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ACUTE BENIGN PERICARDITIS OF UNKNOWN ORIGIN

BY

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Received September 18, 1951

Since the earliest description of "idiopathic pericarditis" by Hodges in 1854 (Carmichael *et al.*, 1951) occasional records of small series or single cases of a benign form of pericarditis have been reported. Comer (1927) reported a case of pericarditis that he thought to be a sequel of acute sinusitis. Bing (1933) described six examples of a mild form of pericarditis, sometimes associated with pleurisy, clearly distinguishable from rheumatic and tuberculous pericarditis; he believed the disease to be infectious and suggested the title "epidemic pericarditis." The condition attracted little notice until Barnes and Burchell (1942) described its features in more precise detail and established it as a clinical entity. Since then it has been more widely recognized, especially in the United States. Nay and Boyer (1946) found 15 examples of "idiopathic pericarditis" among 46 cases of pericarditis of varied ætiology admitted to an Army Rheumatic Centre. Logue and Wendkos (1948) were of the opinion that the condition was often overlooked and in reviewing 77 cases of pericarditis they found 17 examples of this benign form, 6 of which had been originally diagnosed as cardiac infarction. Feder *et al.* (1950) described 5 cases; they believed the diagnosis was usually missed entirely and that the symptoms, when mild, were usually mistaken for influenza or pleurisy, and when severe, for coronary occlusion. Levy and Patterson (1950), after a study of 27 cases, thought the clinical picture was quite distinctive, the chief differential diagnosis being from cardiac infarction. Carmichael *et al.* (1951) in a full review of 50 cases, found that they had encountered the condition more frequently in recent years.

To date, little attention has been paid to the condition in this country. The following 5 cases illustrate many of the typical features of the condition and show some of the difficulties that may arise in differential diagnosis.

Case 1, a man, aged 34, was first seen in April, 1948. He gave a history that the previous night in bed he had developed a heavy ache behind the mid-sternum but managed to sleep. The pain was still present the next morning, gradually increased in severity and was aggravated by deep breathing.

On examination, temperature 99° F.; pulse regular; B.P. 125/80; the apex beat was not palpable; a loud pericardial rub was heard and there were many rales at both bases.

The pain lasted for two days; on the fifth day the pericardial rub disappeared and the temperature returned to normal. A cardiogram taken on the second day of the illness, was within normal limits, but on the fourth day there were RS–T changes characteristic of acute pericarditis. In a further record, two days later, the RS–T changes had disappeared but the T waves were diminished though positive. Three weeks later the tracing was within normal limits (Fig. 1). A chest X-ray, taken two weeks after the onset of pain, showed no abnormality. He made an uneventful recovery and was well when last seen three years later.

Case 2, a women, aged 18, was first seen in March, 1950. She gave a history that 4 weeks previously she had developed an unproductive cough and a week later woke up one morning with a continuous aching pain behind the mid-sternum. Pain persisted for the next two weeks, becoming severe when she walked, often compelling her to stop. After the first week it became stabbing in character and was aggravated by deep breathing. Malaise and breathlessness commenced as the pain disappeared and the day before her admission to hospital she experienced three severe and alarming attacks of dyspnœa.

On examination she was breathless and orthopnœic; temperature 100° F.; pulse regular and rate 120; the heart sounds were normal but distant; there were signs of pericardial effusion with cardiac tamponade, and a pleural rub was present at the left base behind.

Her dyspnœa and general condition improved following the removal of 50 ml. of blood-stained pericardial fluid, and three days later a pericardial rub was heard; this remained for 10 days. By the seventh day the patient was symptom-free but a low-grade pyrexia persisted till the eighteenth day. Chest X-rays, on admission, showed a moderately large pericardial effusion, which had almost completely re-absorbed by the end of three weeks. A small left-sided pleural effusion cleared rapidly. Serial cardiograms showed T wave changes typical of acute pericarditis and did not return to normal for about 4 months from the onset of chest pain. The pericardial fluid was sterile on culture and guinea-pig inoculations were negative for tubercle bacilli. The highest white cell count was 12,300, of which 76 per cent were neutrophiles. B.S.R., 30 mm. (Wintrobe) on admission, fell to normal in two weeks. Sputum contained many pus cells but no significant organisms. Mantoux reactions 1/10,000 and 1/1,000 were negative six months later. She was in good health when last seen ten months later.

Case 3, a man, aged 22, was first seen in September, 1950. He gave a history that two weeks previously he had developed a pain behind the mid-sternum, which he likened to indigestion. At first this pain was a constant ache but after a few days it became stabbing in character and was aggravated by deep-breathing. It remained thus for the following 10 days.

On examination, temperature 101° F.; pulse regular; B.P. 140/90; the apex beat was not palpable; the heart sounds were normal; a loud pericardial rub was present and also a pleural rub under the left scapula.

The pericardial rub disappeared on the seventh day and temperature settled on the eight day. He was symptom-free by the second week in hospital and made an uneventful recovery. On admission, teleradiograms showed enlargment of the heart shadow and this did not return to normal for six weeks. Serial cardiograms showed RS–T and T wave changes characteristic of acute pericarditis. The tracings remained abnormal for two months (Fig. 2). The white cell count was never greater than 9,000 (66% neutrophiles) and the B.S.R., which was slightly raised on admission, fell to normal in 3 weeks. Sputum contained pus cells but no organisms. Mantoux reactions 1/10,000 and 1/1,000 were negative 3 months after the onset of the illness. He was in good health when last seen 6 months after discharge from hospital.

Case 4, a man, aged 36, was first seen in February, 1951. He gave a history that three weeks previously he began to feel feverish and had developed a constant ache behind the mid-sternum which persisted for a week. The pain then moved to the left chest, became sharp and knife-like and was made worse by deep-breathing and certain movements such as bending towards one side.

On examination, the temperature was 100° F.; the pulse was regular; B.P. 120/80; the apex beat was not palpable; the heart sounds were normal; there was a faint pericardial rub and a pleural rub at the left base.

The pericardial rub had disappeared by the next day, the pleural rub persisted and a small effeusion developed at both bases; these quickly re-absorbed. Temperature rarely rose above 99° F. and settled in the third week. On admission, teleradiograms showed enlargement of the heart shadow with a little fluid in both pleural cavities. The appearances were normal at the end of a month. Serial cardiograms showed changes typical of acute pericarditis, the tracings remaining abnormal until seven weeks from the beginning of the illness. Pleural fluid contained 3·2 per cent protein and the cells were mainly lymphocytes; it was sterile on culture and negative on guinea-pig inoculation. The highest white cell count was 9,000 per cm. (74% neutrophiles); B.S.R., 51 mm. (Wintrobe) on admission, fell to normal in two weeks; cold agglutinins negative and complement fixation tests for influenza A. and B. and for Q. fever were negative, as also were agglutinations for *Streptococcus M.G.* Mantoux 1/10,000 was negative but 1/1,000 was weakly positive. His convalescence was uneventful.

Case 5, a girl, aged 5, was first seen in June, 1951. In February, 1951 she had been in an isolation hospital with measles complicated by pneumonia and followed by impetigo; recovery was complete and she returned to school. Three weeks before her admission in June she was noticed to be listless and a little breathless on exertion. There were no joint pains.

On examination, temperature 99° F.; pulse regular, rate 120; the apex beat was not palpable; there was a loud pericardial friction rub with normal heart sounds. There were no other abnormal findings. A provisional diagnosis of acute rheumatic carditis was made.

In spite of salicylates the temperature rose steadily to 103° F of by the seventh day. Thereafter it began to settle, and remained normal after the end of the second week. The pericardial rub disappeared two days later, the heart sounds remained normal and there were no murmurs. She was fretful for the first 10 days, after which her recovery was rapid and complete. Throughout the illness there were no joint pains or any other signs suggestive of acute rheumatism. Serial cardiograms showed the changes of acute pericarditis with a P–R interval of 0·14 sec. X-rays showed slight general enlargement of the heart shadow, which returned to normal in 4 weeks. The lung fields were clear throughout. The white cell count did not rise above 7,500 (57% neutrophiles, 35% lymphocytes). B.S.R. was 33 mm. (Wintrobe) on admission and

fell to normal after 9 days. Mantoux 1/10,000 was negative on two occasions. This case was exceptional in as much as the illness appeared to be painless throughout.

Little is known of the ætiology of this form of acute pericarditis and it is possible that it may not be the same in all cases. Numerous examinations of blood, pericardial and pleural fluids have failed to demonstrate an infective agent, except in two instances when a hæmolytic streptococcus was recovered from the pericardial fluid (Gardner, 1937; Rizler and Diebowts, 1948). A history of preceding infection, usually in the respiratory tract and often mild and transitory, was noted in about half the cases reported by Barnes and Burchell (1942) and by Carmichael *et al.* (1951) and there are clear accounts of pericardial effusions in young men following acute sinusitis (Comer, 1927) and acute pharyngitis (Willius, 1934). In this series Case 2 developed a dry cough one week before the onset of pericarditis and in both this case and in Case 3 pus cells were present in the sputum. Sometimes the condition appears to follow the common cold and this has led to the supposition that the causative agent may be virus, a view supported by the occasional occurrence of pericarditis in primary atypical pneumonia (Fuller and Quinlan, 1943; Finkelstein and Klainer, 1944).

The whole course of the illness is quite unlike that of acute rheumatism with active carditis and no case has been found to develop subsequent valvular heart disease (Nay and Boyer, 1946). A tuberculous ætiology is more difficult to exclude but evidence of active tuberculosis has always been lacking and the Mantoux reaction has been found negative in a number of cases (Carmichael *et al.*, 1951; Porter *et al.*, 1950 and Levy and Patterson, 1950). The Mantoux was negative in three of the four cases in which the test was done in the present series.

Clinical Features

A number of reports have stressed that the condition usually occurs in young adults; but according to Carmichael *et al.* (1951) this age incidence has been over-emphasized as 18 of their 50 cases were between 51 and 70 years and 14 were under 20 years of age. Pain is almost invariably the presenting symptom; it is usually likened to severe indigestion or a heavy ache. It is commonly felt behind the mid- or upper-sternum and may radiate into one or both shoulders. It lasts a variable time, usually a few days but sometimes persists for a week or more. At first the pain is generally constant but later may be aggravated by deep-breathing and movements of the trunk. Pleural pain may be present as well, sometimes from the onset but more often a few days later; it may be bilateral (Levy and Patterson, 1950) and may be followed by pleural effusion. Fever is usually slight and tends to settle in a week or so. Malaise is generally short-lived and once pain is relieved there is often a remarkably rapid return of well-being, at times in spite of the presence of fluid in the pericardium and both pleural cavities.

A pericardial rub is the important clinical finding. This usually appears early and, therefore, whether it is heard or not depends to a large extent on the stage of the illness when the patient first comes under observation. In published reports a pericardial rub has been recorded in about three-quarters of all cases and has remained present for roughly a week but in one instance persisted for as long as 60 days (Nay and Boyer, 1946; Levy and Patterson, 1950; Feder *et al.*,1950 and Carmichael *et al.*, 1951). If the rub is absent pericardial involvement may be overlooked, especially if a cardiogram is not available. Both pericardial and pleural effusions are common and the former may be blood-stained, as in Case 2 (Nathan and Dathe, 1946; Porter *et al.*, 1950). In the present series a pericardial rub was heard in every case, in four at the first examination and in one it appeared for the first time after paracentesis. In the five cases the rub remained for an average period of 7 days; the longest time was 14 days and the shortest was less than 12 hours.

Recovery is usually quite rapid and at the end of two or three weeks the electrocardiographic changes are often the sole remaining clinical abnormality. The average duration of the illness in one large series was 13 days (Carmichael *et al.*, 1951). Relapses are not uncommon and may occur a month or more after apparent recovery (Burchell, 1947; Levy and Patterson, 1950), in which case

pain, and the signs of pericarditis and pleurisy may all return and cardiographic changes may start afresh.

Laboratory investigations are of little help in the diagnosis, except in excluding positive evidence of active tuberculosis. There may or may not be a polymorphonuclear leucocytosis and the sedimentation rate, at first raised, falls to normal as a rule in the course of two weeks (Burchell, 1947).

X-rays reveal enlargement of the heart shadow in most cases. If the findings in a number of reports are considered together, then out of a sum total of 99 cases enlargement was present in 62 (Wolf, 1943; Nay and Boyer, 1946; Feder *et al.*, 1950; Levy and Patterson, 1950; Porter *et al.*, 1950, and Carmichael *et al.*, 1951). In many instances the presence of pericardial effusion has been proved by paracentesis (Barnes and Burchell, 1942; Levy and Patterson, 1950, and Porter *et al.*, 1950), and in one case the enlarged heart shadow was noted to return to normal after removal of 350 cc. of fluid. At first sight it would appear reasonable to presume that pericardial effusion is responsible for the X-ray changes in all cases, but this premise has been questioned by Wolf (1943), Burchell (1947), Levy and Patterson (1950), and Carmichael *et al.* (1951). These observers believe that cardiac dilatation plays an important part and may be solely responsible for the enlargement in some instances. They point out that considerable enlargement can occur within 12 hours of the onset of pain and that in spite of this rapid increase in size clinical evidence of cardiac compression is uncommon; moreover, the heart sounds may not be diminished and the voltage may remain normal in the electrocardiogram. The evidence in favour of cardiac dilatation is at the moment inconclusive and awaits further investigation. In the present series X-rays demonstrated enlargement of the heart shadow in 4 of the 5 cases. In one the enlargement was considerable and a pericardial effusion was proved by paracentesis. Enlargement was only slight to moderate in the remainder. Final examination showed the heart size within normal limits in each case.

Serial electrocardiograms reveal the typical pattern of acute pericarditis in a large majority of cases. These changes have been shown by Fowler and others (1932) and by Vander Veer and Norris (1939) to be the result of injury to the subepicardial muscle fibres and they characteristically occur in two phases. The first consists of elevation of the RS–T segments, most typically in all three standard leads but often in leads I and II, less often in II and III and occasionally only in either lead I or III. These changes are sometimes transient but usually last a day or so. At this stage the T waves remain upright and are sometimes sharply peaked, the RS–T segments being concave upwards (Barnes and Burchell, 1942). There is rarely reciprocal deviation of the RS–T segments in leads I and III and never QRS changes, such as occur in myocardial infarction, but the QRS voltage may be lowered if a pericardial effusion develops. In the second phase the RS–T segments return to the iso-electric level and the T waves become flattened and usually inverted. Serial cardiograms often show these T wave changes to be unstable, sometimes varying from day to day, and if frequent records are taken it is usual to find negative T waves in all three standard leads at some stage. Occasionally the RS–T elevation is not followed by T wave inversion (Coffen and Scarf, 1946), as shown in the cardiogram in Case 1 (Fig. 1). Chest leads follow the same pattern as the limb leads. Providing there are no permanent sequelae the cardiogram returns to normal usually in the course of six to eight weeks but may remain abnormal for two to three months. The improvement in the cardiogram does not necessarily run parallel with resolution of the pericarditis, the former may become normal even though the latter continues and an increasing amount of fluid is being formed (Vander Veer and Norris, 1939).

In tuberculous pericarditis RS–T changes are rarely seen (Bellet and McMillan, 1938; Vander Veer and Wagner, 1946), and in rheumatic pericarditis Wood (1950) were able to record either RS–T or T wave changes in less than half the cases. This is in sharp contrast to the findings in nonspecific pericarditis. Levy and Patterson (1950) found RS–T elevation in 19 of their 26 cases, in fact in every tracing taken in the first few days of the illness; in 6 cases the changes were limited to the T waves and only one case had a normal cardiogram throughout. The abnormalities remained for an average period of six weeks, the longest for three months. Likewise, of the 17 cases described by Logue and Wendkos (1948) RS–T changes were recorded in 15 and T changes in the

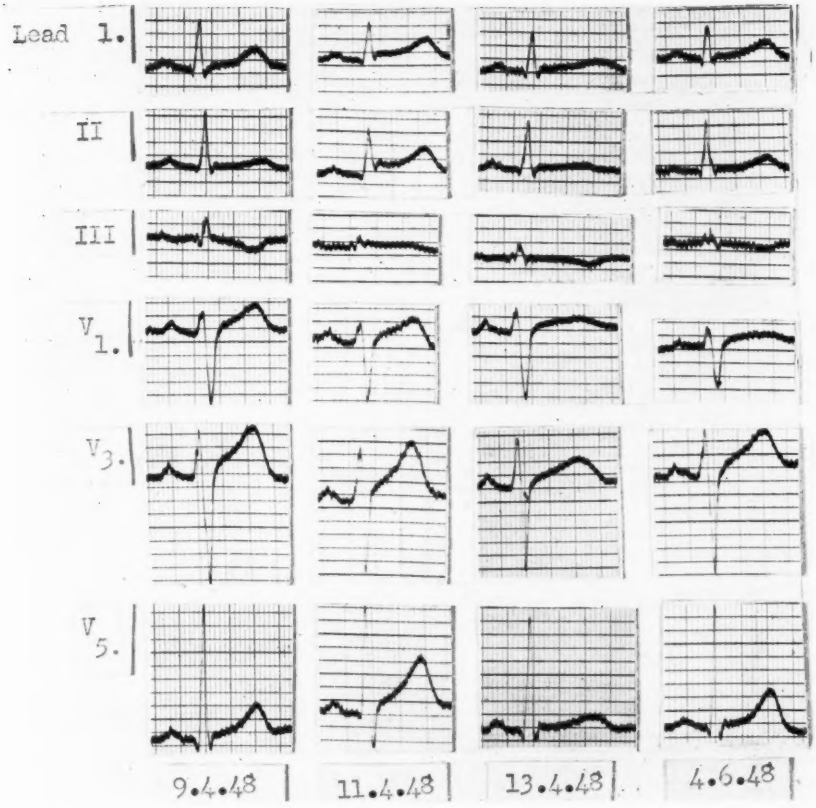

FIG. 1.—Cardiogram in Case 1, showing RS–T elevation in leads I, II and V5. The T waves later became flattened but T wave inversion was not recorded.

remainder. Feder and others (1950) found the cardiogram typical of pericarditis in all their five cases. It should be stressed that the P–R interval was not found prolonged in any of these reports.

In the present series cardiograms were characteristic of acute pericarditis in every case. RS–T elevation was recorded in two (Case 1 and 5) and in another (Case 3), investigated two weeks after the onset of pain, slight RS–T elevation persisted in the presence of T wave inversion (Fig. 2). According to Nay (1949) this association is unusual; he found that in pericarditis as opposed to cardiac infarction, the T waves seldom became inverted until the RS–T segments had returned to the isoelectric level. In Cases 2 and 4 the abnormalities were limited to the T waves. The tracings finally returned to normal in each case after an average period of seven weeks, the limits being 4 and 11 weeks.

DIFFERENTIAL DIAGNOSIS

The main features of this benign form of pericarditis are pain, pericardial friction and often pleurisy. The correct interpretation of these is important because errors in diagnosis may lead to unnecessary invalidism and prolonged observation. Barnes and Burchell (1942) drew attention to the fact that the condition was frequently mistaken for cardiac infarction. In nonspecific pericarditis

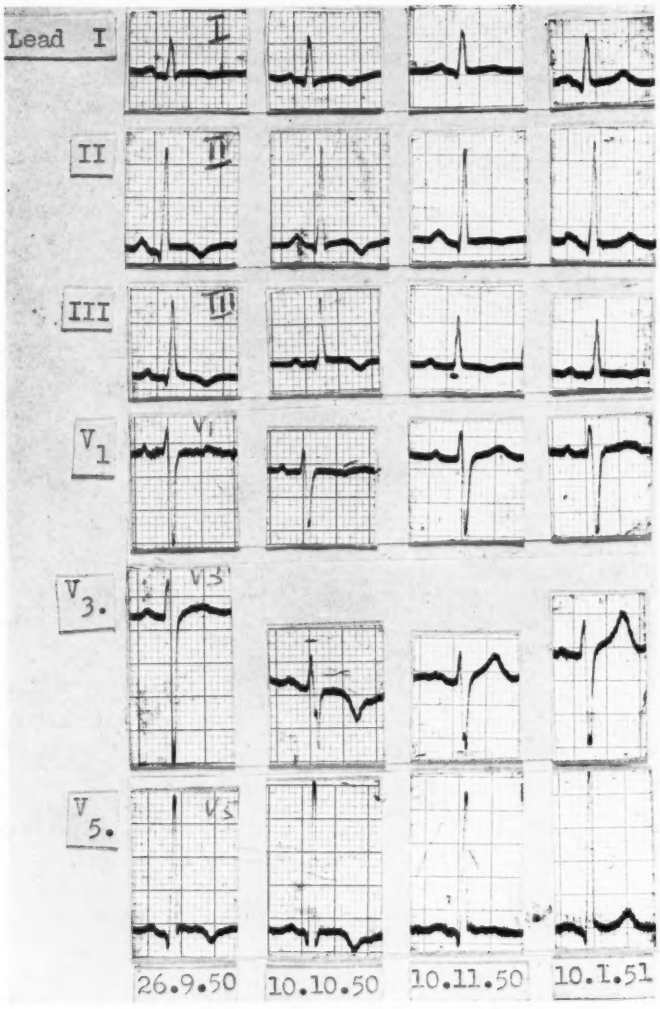

FIG. 2.—Electrocardiograms in Case 3. Inversion of the T waves has occurred before the RS–T segments have returned to normal.

the pain at its onset may closely simulate that of myocardial infarction both in its distribution and character. In the present series all patients were carefully questioned about the character of their pain; Case 5, a girl, aged 5, said she had no pain throughout the illness; in Case 1 the pain remained unchanged throughout except in as much as it was aggravated by deep-breathing on the last day; the three remaining patients all agreed that at first the pain was a constant severe ache felt behind the mid-sternum and quite unrelated to respiration; in the course of days the pain changed in character and became sharp and stabbing and was made much worse by deep-breathing and lying in certain postures, it was completely relieved by holding the breath. It lasted for an average period of 16

days, the limits being 2 days and 4 weeks. Thus it is at the beginning of the illness that the pain may be mistaken for that of cardiac infarction; but if the patient is examined at this stage, the finding of both fever and a pericardial rub so early should make one suspicious.

In nonspecific pericarditis, as opposed to cardiac infarction, shock is rare, often in spite of prolonged pain. This distinction is not infallible (Burchell, 1947), as was witnessed in the case of a 48-year-old man, at present in hospital under observation and not included in this present series: pain was accompanied by severe circulatory collapse, the clinical picture closely simulating that of a severe cardiovascular injury.

An isolated cardiogram may be confused with that due to cardiac ischæmia but serial records are nearly always decisive, as nearly every case shows the progressive changes of acute pericarditis (Nay and Boyer, 1946; Levy and Patterson, 1950, and Feder *et al.*, 1950). In fact, in Case 1, the diagnosis was at first thought to be cardiac infarction and a cardiogram, taken 36 hours after the onset of pain, was quite normal but serial records from the fourth day onwards were characteristic of acute pericarditis.

Acute non-specific pericarditis differs from tuberculous pericarditis both in its onset and subsequent course. The onset of the former is usually sudden and the chief complaints are pain and malaise, both of which may subside, often with unexpected suddeness, in the course of a week or so. This almost abrupt disappearance of distressing symptoms, with the restoration of a feeling of well-being, occurred in four of the cases here described. On the other hand, in tuberculous pericarditis pain is rarely a prominent feature; the onset is usually insidious and dyspnœa and cough are the common presenting symptoms (Clarke, 1929; Porter, 1945). The pericardial fluid may be blood-stained in both conditions and the cellular reaction mainly mononuclear in both pericardial and pleural fluids. If serial cardiograms are taken early in the course of the disease RS–T changes are usually found in non-specific pericarditis but rarely when the infection is tuberculous (Vander Veer and Wagner, 1946). The Mantoux reaction is helpful if persistently negative. Case 2 was too distressed on admission to hospital to give an account of her illness. She presented with a large blood-stained pericardial effusion, thought at first to be tuberculous. This, however, seemed unlikely when a full history was available, and was finally excluded by the course of the illness.

Acute rheumatic carditis has to be excluded, particularly in young subjects who have a history of recent upper respiratory infection and develop signs of pericarditis with X-ray evidence of cardiac enlargement. However, in non-specific pericarditis joint pains, signs of valvular damage, or disturbances in auriculo-ventricular conduction do not occur. Moreover, salicylates do not influence the temperature or the symptoms of the disease in any way. Case 5 was initially diagnosed as having acute rheumatic carditis but this had to be revised in view of the failure of salicylates to affect the rising temperature, the absence of joint pains, the progressive S–T and T changes with normal auriculo-ventricular conduction and finally the rapid and full recovery without any heart murmurs.

If, when the patient is first seen, signs or pericarditis have disappeared but a lymphocytic pleural effusion is present, this last finding may be sufficiently misleading to suggest a diagnosis of primary tuberculous pleurisy. In these circumstances pericardial involvement may be overlooked entirely without the help of X-rays or cardiograms. When Case 4 was admitted to hospital the only abnormal findings were a pleural rub under the left scapula and signs of fluid at the left base. A pericardial rub heard the previous day had disappeared by the same evening. It is possible that more examples of non-specific pericarditis would be found if all cases of transient pleural effusion of obscure ætiology were investigated by means of serial cardiograms.

Lastly, there is the problem of the patient seen four or six weeks after an illness characterized by severe retrosternal pain, revealing no abnormalities on physical examination but with T wave inversion in the electrocardiogram. In benign pericarditis T wave inversion may persist for two or three months (Feder *et al.*, 1950), but there are no QRS changes of cardiac infarction, and with full awareness of the cardiographic pattern of acute pericarditis the problem should present no great difficulty.

Prognosis and Treatment

The prognosis in acute nonspecific pericarditis is excellent and so far the only fatality that has been reported occurred in a patient mistakenly diagnosed as having an acute cardiac infarct and given anticoagulant therapy. This treatment may have been responsible for the hæmopericardium found at autopsy (McCord *et al.*, 1951). No case, as yet, has developed signs of constrictive pericarditis, but it is of interest that Carmichael and others (1951) found calcification in the pericardium of one patient four years after the initial illness.

The disease appears to be self-limiting, and symptomatic treatment is usually all that is needed. Taubenhaus and Brams (1950) tried the effect of aureomycin in three cases and claimed a dramatic response; but sudden improvement often takes place spontaneously in untreated cases, as, in fact happened in Case 4, at the time when aureomycin therapy was being considered. Penicillin, streptomycin, and sulphonamides have proved of no value (Levy and Patterson, 1950). Cardiac tamponade is rare but it occurred in Case 2, and has been previously described by Burchell (1947); both these patients needed pericardial aspiration, but this is exceptional.

Summary

Five examples of a benign form of acute pericarditis are described.

The onset of the condition is usually sudden and pain is the predominant symptom; this may simulate that of cardiac infarction. Fever and a pericardial rub are important early signs. Pleurisy is common and there may be effusions into both pericardial and pleural cavities. Recovery is usually complete in two or three months, but relapses may occur.

The condition has to be distinguished from rheumatic and tuberculous pericarditis, from primary pleurisy and from myocardial infarction.

The importance of serial cardiograms and X-ray findings are discussed.

I wish to thank Dr. F. O. MacCallum of the Virus Reference Laboratory, Colindale Avenue, London, N.W.9, for his help with the pathological investigations in Case 4.

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COR BILOCULARE

BY

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The heart with only two chambers, the cor biloculare, is rare and the following case that was fully investigated in life seems worth reporting.

D. O. (Case O136), aged 5 years at the time of his death, was the youngest of three brothers of whom the other two are well. His mental development was normal and he was talking by 18 months, but his physical development was slow for he did not walk till 30 months and was always below normal size—2 ft. 10 in. in height and 24 lb. in weight at 3 years, and 3 ft. 2 in. in height and 34 lb. in weight at 5 years.

He was seen by us when 3 years old (1948) and at frequent intervals from then until his death two years later; as there was no great change in his condition, the notes of the different visits have been combined. He was a puny child with rather frequent attacks of bronchitis. His chest was deformed, the left side being prominent and the lower half of the sternum bent sharply backwards.

He was much disabled and breathlessness prevented him walking more than 25 yards. There was no history of squatting. Cyanosis had been present since birth, slight at first but increasing a little during his last two years; there was only slight clubbing of the fingers. Corresponding with these findings, his polycythæmia was only moderate but had been increasing, his hæmoglobin having risen from 118 to 139 per cent shortly before his death, with 8·7 million red cells and a hæmatocrit of 73 per cent.

A continuous murmur that sounded rather superficial was heard over the upper left chest especially in the first and second spaces in front, in the left axilla, and over the left but not over the right side behind. The thrill was fine and only systolic. The second sound in the pulmonary area was loud and single. His blood pressure varied between 90/50 and 105/75.

The heart was moderately enlarged and rather horizontal with a cardio-thoracic ratio of 57 per cent (9·5/16·8 cm.) (Fig. 1A). It was sabot-shaped with a fairly deep pulmonary bay that was made less obvious by the very broad pedicle. The right ventricle was much enlarged, though less prominent in the left oblique view than is usual in Fallot's tetralogy because of the anterior position of the aorta: the left ventricle also was thought to be enlarged. The aorta arched normally to the left side: it pulsated forcibly and it was wide and uncoiled so that a truncus arteriosus was thought probable at one time, but later a left pulmonary artery was certainly seen, and probably a smaller right, though these were rather hidden in films because of the shape of the heart : their origin was not seen.

The electrocardiogram appeared to show right ventricular preponderance and this was confirmed by chest leads, R in V1 being nearly 40 mm. with an insignificant S, and R remaining of moderate size till V5 (Fig. 2). There was no T inversion beyond V1 where it was only slight. There was a variable pacemaker, P in leads II and III often being small and inverted, and at times there was a change to nodal rhythm, with P just after QRS with very little change of rate. In one record there was some S–T elevation, probably caused by a variable degree of anoxæmia.

Although the heart was in its normal position on the left, the stomach was found to be on the

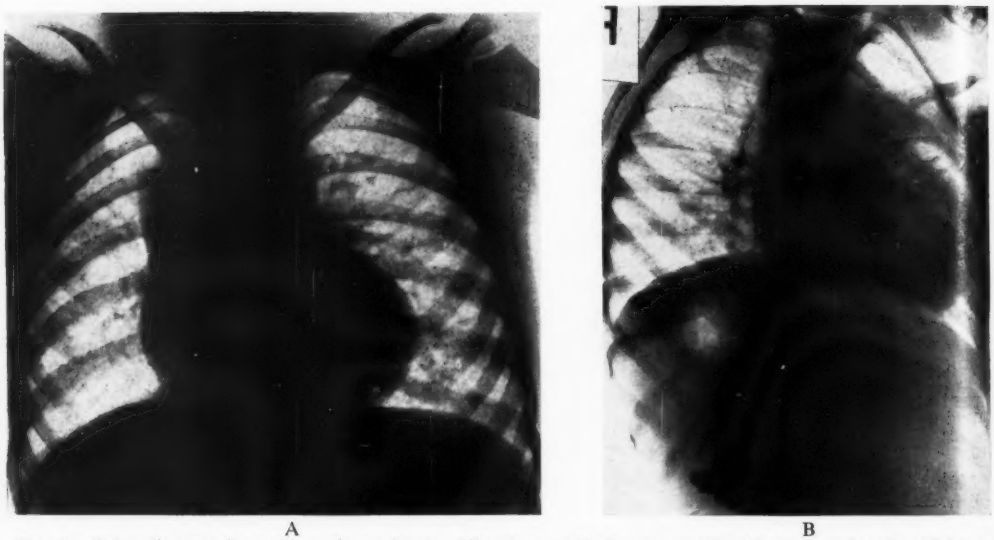

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FIG. 1.—Teleradiogram from this patient with cor biloculare. (A) shows a moderately large sabot-shaped heart. The extremely wide pedicle was composed of a very horizontally placed aorta and bilateral superior venæ cavæ, one of which was joined by a large azygos vein. (B) Right anterior oblique position. The barium shows the stomach to be on the right, and there was lævocardia with situs inversus of the abdominal viscera.

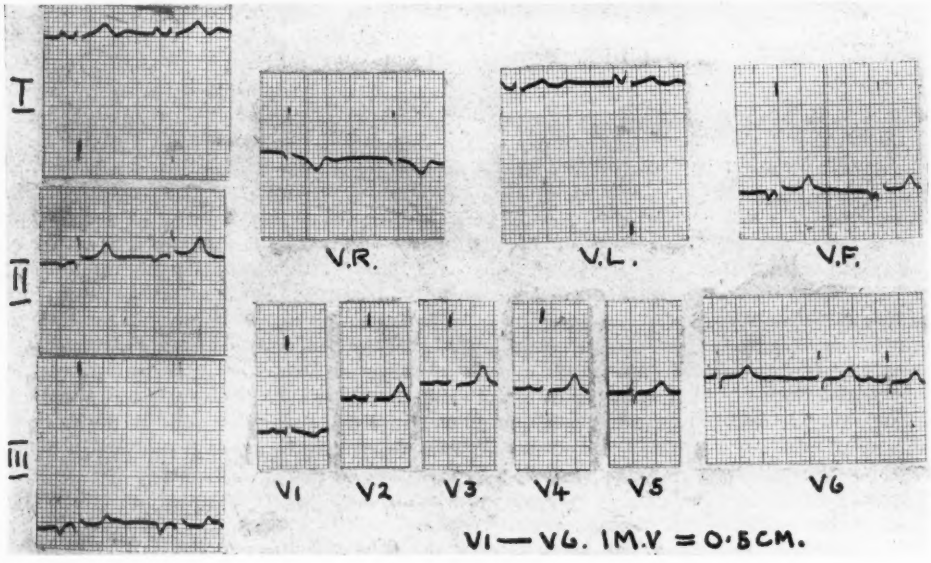

FIG. 2.—Electrocardiogram from this patient with a single ventricle. It appears to show all the features of right ventricular preponderance—gross right axis deviation, a large R in VR, a vertical heart, a large R of 40 mm. and an insignificant S in V1 and R remaining larger than S all across to V6, but becoming small in V5 and V6. Standardization 1 mv.=0·5 cm. for chest leads. Where they are very fine the tips of the waves have been marked.

right (Fig. 1B) and the liver on the left side, so that it was likely that the defect of the heart would be complex. The clinical diagnosis was pulmonary atresia with the blood supply to the lungs through bronchial or other collateral arteries that anastomosed with the small pulmonary arteries beyond the atresia. There were no signs of congestive failure.

Angiocardiography. An atrium and ventricle on the right filled readily and at 1¼ *sec. the aorta and its branches were already well filled* (Fig. 4). At 2¼ sec. the heart shadows were already fading, the aorta was very dense, and *both pulmonary arteries, especially the left, were seen fairly well though how they were filling was not obvious* (Fig. 3B). At 3¼ sec. the lungs were filling, the left better than the right, and the pulmonary arteries were now as dense as anything else. From then on the shadows only changed slowly and the left side of the heart was not seen to fill again from the pulmonary veins.

Cardiac catheterization. This proved difficult and neither from the left nor from the right arm could the catheter be passed further than the right and left innominate veins, samples from which had an O_2 saturation of 54 compared with 63 per cent in the femoral artery.

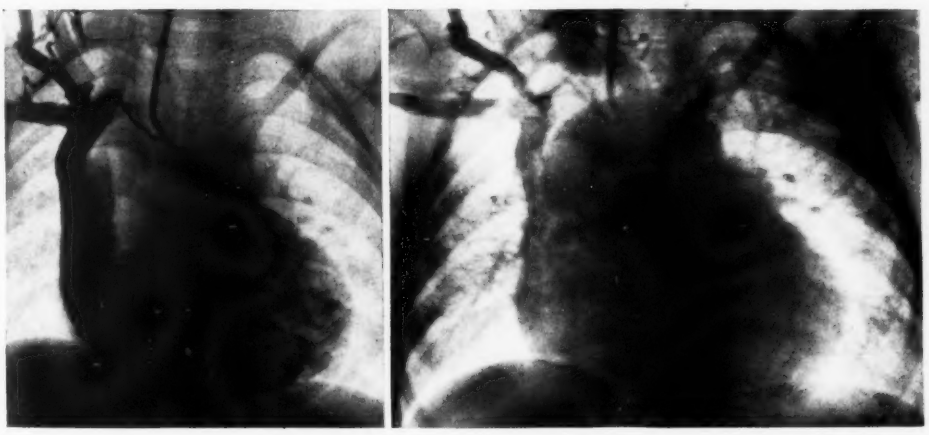

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FIG. 3.—Angiocardiograms showing the unusual filling of the heart and the very horizontal aorta. (A) At ¾ sec. the diodone is mostly on the right and spreading across to the left. The absence of a sharp border to the "right" ventricle might have suggested a single ventricle (see also Fig. 4). At 1¼ sec. the aorta was well filled and this is shown in Fig. 4 where the diodone had been injected from below. (B) At 2¼ sec. the heart shadows have begun to fade, but the aorta is still well seen. The pulmonary arteries, especially the left, are beginning to show but how they are filling is not clear.

Finally the internal saphenous vein was used. The catheter passed straight up past the heart and turned down into the superior vena cava to enter an atrium on the right. Evidently it had passed up a large azygos vein (see Fig. 4)—a vessel that is better known as a collateral channel when the inferior vena cava is obstructed than as a congenital abnormality carrying most of the blood from the lower part of the body.

The samples that were supposed to be from the atrium were, in fact, from the azygos vein. The blood from the ventricle was much more oxygenated (68–70%) than that from the azygos vein (40–44%) or that taken on an earlier occasion from the jugular vein (54%), suggesting that there was also a left-to-right shunt through a ventricular septal defect. The mean pressure in the ventricle was 60 mm. Hg. The pulmonary artery was not entered. Estimations on separate occasions suggested a peripheral flow of 5·2 litres a minute and a pulmonary flow of 1·5 litres but the circumstances were too different to allow any conclusions about the size of the right-to-left shunt.

Because of the abnormality of the veins, diodone was injected with the catheter in the azygos vein. The atrium filled only through the azygos vein (Fig. 4), which took its normal course although it was performing nearly all of the functions of the inferior vena cava. The hepatic veins, however, did join the atrium in the normal site, as was shown by their filling by backward flow from the atrium at 1 sec. (Fig. 4) but not earlier from the azygos vein.

FIG. 4.—Angiocardiogram after injection into the azygos vein. Diodone is seen passing up the azygos vein to enter the superior vena cava which appeared to be the only venous route to the heart from the lower part of the body. After 1 sec., the right side of the heart was well filled and diodone was passing across towards the left side and filling the horizontally placed aorta. The descending aorta is about the same size as the azygos vein. The hepatic veins have filled from the atrium on the right.

Course and operation. The final diagnosis was pulmonary atresia with a large ventricular septal defect. Pulmonary arteries were thought to be present beyond the atresia but it was not certain how they were supplied. The visible pulsation in the neck and in the aorta on radioscopy favoured a patent ductus arteriosus but no pulsation was seen in the pulmonary arteries: the superficial quality of the continuous murmur favoured bronchial arteries though neither the dense diffuse shadows high in the mediastinum nor the nodular shadows at the hilum of the lung that are characteristic of this blood supply to the lungs were seen (Campbell and Gardner, 1950). There was also an azygos vein draining most of the lower part of the body.

It was thought that the blood flow to his lungs was diminished, and that the child would, therefore, benefit by a Blalock-Taussig operation. On July 29, 1950, Mr. R. C. Brock did an end-to-end subclavian-pulmonary anastomosis, and found that there was pulmonary atresia and a patent ductus arteriosus with a thrill in the left pulmonary artery just below it. After the operation the patient's colour improved, but he took a long time coming round from the anæsthetic and remained unusually drowsy. Next morning he seemed better, but died suddenly.

POST-MORTEM FINDINGS

Cor biloculare; single atrium; common A–V orifice; single ventricle. Pulmonary trunk atresic, but right and left pulmonary arteries supplied by a patent ductus arteriosus on the left side. Aorta arising from common ventricle without a rudimentary chamber. Absent inferior vena cava. Large azygos vein draining the lower part of the body. Persistent bilateral superior venæ cavæ, the right receiving the azygos vein, and the left entering the atrium through the coronary sinus.

The azygos vein entered the superior vena cava on the right side in its normal position; it was formed by the junction of the common iliac veins and received all those tributaries that normally join the inferior vena cava,* except the hepatic vein which alone entered the atrium in the normal position. A left superior vena cava was also present, and entered the atrium through a greatly dilated coronary sinus. These changes explained the broad pedicle of the heart. There were no venous valves except a probable remnant of the sinus septum over the coronary sinus. The pulmonary veins from each lung joined into one vein and the two veins, one from the right and one from the left lung, entered the common atrium close together.

The heart weighed 180 g. (Fig. 5). There was a single atrium (Fig. 6). This had a vertical

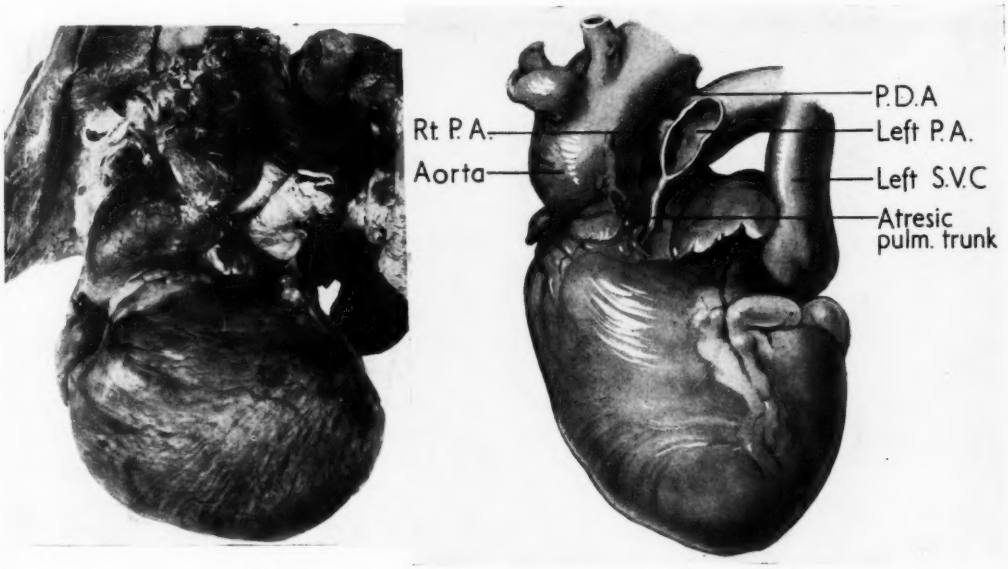

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FIG. 5.—The heart and main vessels. In the photograph (A) the lungs and descending aorta have been turned upwards. The wide rather horizontal position of the aortic arch is well shown. The pulmonary artery is not visible as it is behind the aorta. The curious linear arrangement of the muscle fibres spreading out fanwise from the upper left border is well shown. In the drawing (B) the arrangement of the main vessels can be seen more clearly and they have been spread out for this purpose.

ridge on its superior and anterior walls; Professor Whillis kindly examined the heart with us and thought that it neither looked nor felt like a septum primum but was probably a remnant of the septum spurium. This ridge ended opposite the middle of the common atrioventricular orifice.

The common atrium communicated with the common ventricle through a single, rather oval valve that was 20 mm. in its longest diameter. When the cusps are abnormally formed it may be difficult to decide how many there are, but here the valve had a somewhat rectangular shape suggestive of four valve cusps, though these were not well demarcated from each other and the chordæ tendineæ were not arranged in four separate insertions. There was only one commissure, lying below the left auricular appendage.

There was a single ventricle with no trace of any muscular septum though there were many trabeculæ. It was rather globular in shape and with a raised apex. The superficial muscle fibres

* We have recently seen another patient where cardiac catheterization demonstrated this abnormality.

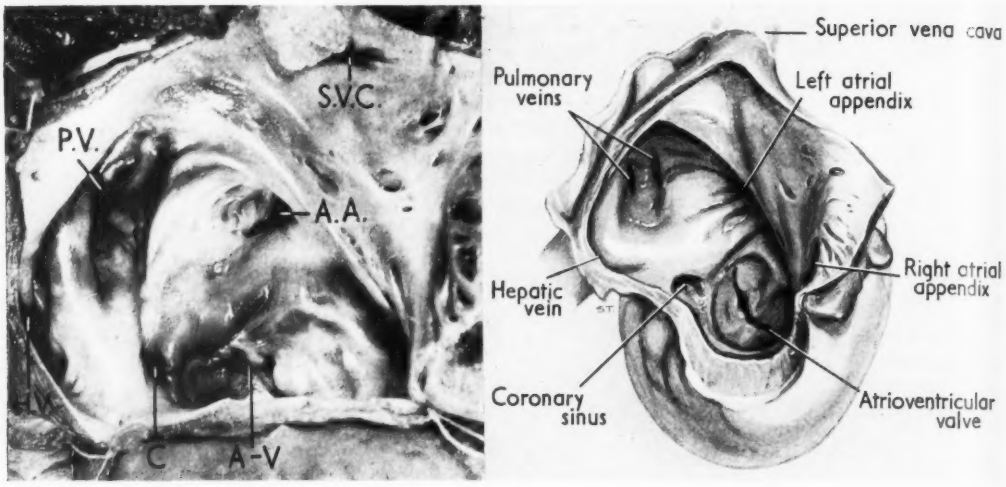

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FIG. 6.—The common atrium has been opened and its walls turned back so that the openings into it can be seen. In the photograph (A) the letters stand for the openings marked on the drawing (B).

fanned out in a curious manner across the anterior surface of the ventricle from its left border, those near the apex running circularly and those nearer the base turning up towards the atrioventricular junction (Fig. 5). The ventricular wall varied in thickness, being 12 mm. anteriorly, 8 mm. at the apex, and 6 mm. posteriorly. One raised band of muscle lay beneath the left border of the anterior wall and another lay between the atrioventricular and aortic valves (Fig. 7).

The aortic valve was normal with two anterior cusps and one posterior cusp; the orifice was 12 mm. in diameter. The large aorta (30 mm. in diameter) was the only vessel leaving the heart. A small dimple, immediately to the left of the aortic valve, marked the site of the pulmonary trunk; this was atresic throughout its length, but the right and left pulmonary arteries were widely patent the left (8 mm.) being considerably larger than the right (5 mm.). A patent ductus arteriosus, 7 mm. long and 4 mm. in internal diameter, opened into the left pulmonary artery near its origin. Just distal to its aortic orifice was a well marked semilunar ridge.

The left coronary artery arose from the left anterior sinus and the right coronary from the posterior sinus. Their distribution was normal. The vessels from the arch of the aorta arose normally.

No gross cerebral lesion was revealed. There was a mild purulent bronchitis. The stomach was in the right side of the abdomen, as was the spleen, which was composed of four separate lobes with other small bodies of splenic tissue lying along the splenic vessels. The liver was central without its shape indicating whether it also was transposed, but its peritoneal attachments showed that this was so.

DISCUSSION

Cases of congenital heart disease with a single ventricle are not very uncommon. More rarely, a single ventricle may be associated with a single atrium—the true cor biloculare which is one of the most primitive types of cardiac defect. Abbott (1936) included 14 examples among her 1000 cases.

In cor biloculare there is a common A-V orifice and valve, sometimes with the four primitive cusps: there are often other defects as well. Abnormalities of the pulmonary veins are often found

FIG. 7.—The single ventricle has been opened by an incision the direction of which lay between its long axis and the vertical line, and the two halves have been opened out to show the interior. The apex lies to the right. Near the top of the cavity the opening of the aorta can be seen (A); it was not obstructed but the valve flaps have protruded downwards in opening up the heart. In the dark shadow just to the right (B) a dimple was all that represented the site where the pulmonary artery should have opened. Two muscle strands can be seen crossing the heart horizontally, the upper perhaps representing the crista supraventricularis. Below this a single cusp of the common A-V valve can be seen.

with gross defects of the atrial septum, and a truncus arteriosus that has not divided into an aorta and pulmonary trunk is often found with a single ventricle, because embryologically the division of these two parts takes place at the same time. The bilocular heart is, therefore, often associated with both these abnormalities, and with a persistent left superior vena cava, this last because the original more symmetrical arrangement on the sinus venosus has been maintained.

Brown (1950) states that the true bilocular heart is rare and that most of the reported cases are partial examples, often with other abnormalities as well. He divides them into (1) complete forms with an undivided truncus arteriosus, (2) complete forms with the aorta and pulmonary trunk divided and (3) incomplete forms where there is some septal formation but a persistent common A-V valve. This case is an example of his type (2).

The common A-V valve is an essential feature of the true bilocular heart, but also occurs with moderate division of the atria or ventricles or of both as the persistent ostium atrioventriculare commune. Half of the forty reported cases of this defect have occurred in mongols. Evans (1950) has, however, pointed out that a large variety of congenital heart defects occur in mongols, this abnormality being relatively uncommon.

Some of the reported cases of cor biloculare show interesting parallels to our case. Kugel (1932) reported one where there was a partial situs inversus of the abdominal viscera, a common A-V orifice with four cusps, atresia of the pulmonary trunk which arose behind the aorta,

pulmonary arteries that were supplied through a patent ductus arteriosus, but with a right-sided aortic arch, and an anomaly of the pulmonary veins which in this case entered the atrium on the left by a common trunk.

The case of Rossman (1942) was very similar. The heart was on the left but there was situs inversus of the stomach and liver with incomplete rotation of the intestine: there was agenesis of the spleen and spina bifida. The superior and inferior venæ cavæ entered a single atrium by a common opening and there were two pulmonary veins. The single A-V orifice had four cusps, one large and three small. The aorta and pulmonary trunk were thought to be transposed in position but the latter was only a fibrous remnant and the pulmonary arteries were supplied through a patent ductus. There was a rudimentary muscular ventricular septum.

Taussig (1947) describes two cases. In one (p. 295) there were two A-V orifices, which is unusual, and the rudimentary chamber in the single ventricle was separated by a muscular ridge; the aorta and pulmonary trunk both arose from this but were partly transposed, i.e. the aorta arose in front: the spleen was absent. In her second (p. 510) the patient had dextrocardia with situs inversus; the aorta and pulmonary artery both arose from a single ventricle and there was pulmonary stenosis: it is interesting for comparison with our case that the inferior vena cava could not be traced to the heart, and the hepatic veins entered the atrium separately but near the pulmonary veins.

In the case of Shechter and Meranze (1944) the heart was on the right but the viscera were not transposed. There was a single atrium with two appendages, a single A-V orifice with three cusps, two large and one small. A large pulmonary trunk and, to the right of this, a much smaller aorta which was joined by a large patent ductus arteriosus arose from the single ventricle.

Nelson and Wells (1948) described a patient who lived 27 years: post-mortem, there was almost complete situs inversus, a spleen that was made up of two lobes, a bilocular heart with a common A-V orifice (with two valve cusps), and transposition of the aorta and pulmonary trunk; there was, however, a rudimentary chamber in the left lateral wall of the ventricle, but neither of the great arteries arose from it. The case of Popjak (1942) showed a common A-V orifice with four cusps, a solitary aortic trunk, and right and left pulmonary arteries supplied through a patent ductus. That of Bembenista (1946) showed a small pulmonary artery arising from a rudimentary chamber that was almost isolated from the main chamber, so that the blood supply to the lungs was mainly through the patent ductus.

Although, in our case, a correct diagnosis of some of the anatomical abnormalities was made, cor biloculare was not thought of. A single ventricle might have been suspected because of the absence of any sharp border of the right ventricle in the angiocardiograms and the way in which the diodone passed across to the left (see Fig. 4); but the left to right shunt at this site did not help greatly as this is fairly common with Fallot's tetralogy. The special problem raised by the heart remaining on the left when the abdominal viscera are transposed is not being discussed here, as we hope to report some other examples of this abnormality.

As in many cases with a single ventricle, the electrocardiogram appeared to show right ventricular preponderance.

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EFFECT OF POSTURE ON VENOUS VELOCITY, MEASURED WITH $^{24}NaCl$

BY

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The importance of posture in the venous return to the heart from the lower limbs in normal and pathological conditions has been recognized for over a century. As early as 1826, Piorry noted that the effect of gravity could produce syncope in subjects kept in the upright posture and that the attack was relieved when the patient lay down. Marshall Hall (1832) carried out animal experiments which showed that the venous return was, to a great extent, dependent upon posture and that the blood in the limbs was directly controlled by gravity. In man, a clue to the mechanism whereby blood is propelled from the lower limbs against the force of gravity is given by the presence of valves in the veins, an adaptation unnecessary in animals that have not assumed the upright gait.

At the same time that these concepts of circulatory control were being investigated, the importance of venous stasis as a factor in the onset of thrombosis was being emphasized. For many years experimental observations on blood flow in the lower limbs have been made both to investigate what conditions may modify venous velocity and also what are the best modes of preventing the occurrence of venous thrombosis.

The methods for measuring such flow-rates have been many and varied, but it was not until the introduction of radioactive substances that a direct and simple technique could be devised. The following observations not only support and amplify the results obtained with earlier and less direct methods, but also give mean flow-rate values under various postural conditions compared with a *standard*, the repeatability of which is discussed.

Methods. The technique of measuring venous flow-rates in the legs was identical with that previously described (Wright *et al.*, 1948; Osborn and Wright, 1949). Briefly, a small volume (0·2–1·0 ml.) of physiological saline containing 2–5 μc. of ^{24}Na is injected intravenously in the foot under standard conditions of temperature, rest, and posture. Through the use of a screened Geiger-Müller counter placed over the femoral triangle, the injected material is detected in the venous stream when it arrives at the groin. By means of a suitable circuit, impulses from the counter are recorded on a kymograph drum, the tracing from which shows the moment of injection, the instant when the radioactive substance passes under the counter, and a suitable time marker. From these data, the distance between the point of injection and the femoral triangle having been measured, the mean rate of venous flow can be deduced.

For each of the following groups of cases, the *standard* flow-rate was recorded for each subject under controlled conditions (Wright *et al.*, 1948). To insure comparable results, the subject rests for 20 minutes with the legs immersed to the knees in a water bath at 40° C.: at this temperature, vasodilation is complete. The subject lies flat in the supine position with the heel at the same level as the heart while the injection is made and the tracing obtained. For comparison with the observation made under these *standard* conditions, the *test* measurement was made immediately afterwards

through the same needle which was left *in situ* in all cases except those of Groups 1 and 2. Normal subjects, men and women, were used for each group of observations; their ages ranged from 16–57 years. No subject suffering from varicose veins was included.

The conditions under which venous flow-rates in the legs were investigated were as follows.

1. Repeated observations in the same leg at weekly intervals, under standard conditions.
2. Comparison of flow-rates of right and left legs on a single occasion, under standard conditions.
3. Comparison of flow-rates in standard (lying) and standing positions.
4. Comparison of flow-rates in standard and sitting (legs down) positions.
5. Comparison of flow-rates in standard and crossed-knee sitting positions.
6. Comparison of flow-rates in standard and head down lying positions, the body inclined at 10 degrees to the horizontal.
7. Comparison of flow-rates under standard conditions before and after vigorous dorsi- and plantar- flexion of the foot for 2 minutes.

Results

The findings for the first two groups of observations, with their standard errors and co-efficients of variation are set out in Table I. These are based upon 48 individual measurements made on 4 normal volunteers, whose venous flow-rates in both right and left legs were measured on each of six occasions under standard conditions.

TABLE I

Flow-rate in 4 Normal Subjects

Subject	Right leg		Left leg	
	Flow rate, cm./sec.	Co-efficient of variation (%)	Flow rate, cm./sec.	Co-efficient of variation (%)
1	5·1±0·45	20	4·6±0·30	15
2	2·5±0·11	10	2·6±0·24	21
3	3·9±0·24	14	3·8±0·40	24
4	5·3±0·25	11	5·6±0·38	15
Average	4·20		4·15	

It can be seen that, while the observations made on the two legs are in every instance closely similar, the flow-rates vary very considerably from one subject to another. The coefficient of variation gives a measure of repeatability on different occasions and this is of such an order that these observations may be said to fall within the same statistical group. When larger groups of measurements are analysed, the average flow-rates are found to agree remarkably closely under standard conditions as shown by the average results of 4·2 cm. sec. in Table I and by the findings for the various groups in Table II.

The extent to which changes in posture (Groups 3–7) alter the flow-rate from that in the standard recumbent position is shown in Table II. Fifteen sets of paired observations were made for each group, from which data the averages and standard errors were derived. The probability (p) that the paired values were significantly different was calculated by Fisher's method.

The paired material shows highly significant differences in every group except the crossed-knee sitting position (Group 5). It is noteworthy that the venous velocity was diminished in both the standing and the sitting (legs down) positions while the reverse, an increased velocity, occurred in the head-down position and after foot exercises.

TABLE II

FLOW-RATE IN VARIOUS POSITIONS

Group	Flow rate (cm./sec.) *standard* position	Flow rate (cm./sec.) *test* position	*p*
3 Standing	4·12±0·54	2·62±0·30	<0·01
4 Sitting	4·70±0·48	3·03±0·34	<0·01
5 Sitting, crossed knees ..	4·70±0·56	5·45±0·76	0·2>*p*>0·1
6 Head down	4·77±0·40	9·11±0·51	<0·01
7 Foot movement ..	3·94±0·31	9·39±0·44	<0·01

DISCUSSION

From time to time it has been suggested that variations in the venous flow-rate in the lower limbs are responsible for local stagnation and hence the far greater incidence of thrombosis in these blood vessels than in those of the arm. Clinically it has been stated that such thrombotic complications occur more commonly in the left than in the right leg. The following short table (Table III) sets out a few of the available series analysed from this view point. It must be stressed that these figures are based on clinical observations and not on autopsy findings.

TABLE III

SITE OF VENOUS THROMBOSIS IN CASES OF PULMONARY EMBOLISM

Author and Year	Right leg (%)	Left leg (%)	Both legs (%)
Cordier, 1905	5·5	92	2·5
Atkins (own and collected figures), 1938	20	66	14
Barker *et al.*, 1941	28	62	10
Wright (unpublished), 1951	37	50	13
Zilliacus (1946)	33	57	10

The explanation put forward for this difference between the two sides is based on anatomical considerations. The sigmoid colon and the common iliac artery are stated to press upon the left common iliac vein, thus causing venous occlusion of varying degrees. The consequent retardation of venous velocity on that side might, therefore, be favourable to thrombus formation. Careful autopsy examinations, however, have not revealed that the incidence of thrombi is, in fact, more common on the left than on the right; indeed, Hunter *et al.* (1941) in his large series found a slight preponderance on the right (206:191), while Ingram (1942), though without giving figures, states that in his series of autopsies, thrombi were discovered as frequently on the right as on the left. We have obtained from the post-mortem reports of cases dying of pulmonary embolism during the past five years (1947–51) in two of the large London Teaching Hospitals (Guy's and U.C.H.) the number of emboli ascertained to have arisen from the two sides of the body. Of 106 deaths recorded, the embolus originated in the right leg in 60 instances while only 46 had come from the left. Such figures do not, of course, constitute any proof that thromboses are more common in the right leg than in the left, but they do suggest that the clinical and autopsy figures may be different. It may be that the typical signs of thrombosis are for some reason more easily recognized during life when they occur on the left side.

Measurement of flow-rates in the two lower limbs has not disclosed any abnormal slowing of the blood stream on the left. Kvale and Allen (1939), using the magnesium sulphate method, found a mean leg–tongue time of 34·28±0·85 sec. on the right, and of 34·0±0·85 sec. on the left. Our more direct method of measuring venous flow-rates has failed to show any significant difference between

the two sides (see Table I), the right giving an average of 4·20±1·3 cm. sec. and the left, 4·15±1·8 cm. sec. It seems unlikely, therefore, that any observed preponderance of clinically diagnosed thrombi in the left leg can be directly referable to any inherent difference in venous velocity on the two sides.

In experimental work, repeated observations on the same subject on different occasions are frequently made. It was necessary, therefore, to determine the variability of our method and to have some measure of the day to day fluctuations that might be expected. For this purpose four volunteers were examined at weekly intervals for six weeks, the observations being made under standard conditions on each occasion. Fishberg *et al.* (1932–33), using the saccharine method, showed that variations in repeated tests on his series of 162 subjects were small. Esser and Berliner (1943) on the other hand, using the same technique, came to the opposite conclusion; their observations, made on 60 patients, 26 of whom suffered from heart disease, showed that when paired tests were performed, similar results were obtained in 6 instances only, while the others showed differences ranging from 1–143 per cent of the initial time. Our observations show a much smaller variation than theirs, the greatest being 27 per cent change between paired measurements. This variation is small when compared with the range of normality found in a large series of volunteers (Wright *et al.*, 1948). We feel, therefore, that, while it is doubtful whether differences of a few per cent are of any significance in any single subject, it is nevertheless justified to regard similar changes in average flow-rates as of greater reliability where the data are obtained from groups.

Interest has been taken in the past in the changes produced in flow-rates by variations in posture. All published figures show a slowing of the venous flow-rate when the subject rises from the lying to the standing posture. Thompson *et al.* (1928), using the brilliant vital red method, showed that in their series, the arm-foot time changed from 45–60 sec. in the recumbant position to 120–150 sec. when the subject stood up. In the following year, Bock *et al.* (1930), using the histamine technique, obtained comparable results, while more recently, Kvale and Allen (1939) and Kvale *et al.* (1940), have further confirmed these observations. Much other supporting evidence on the hæmodynamics of postural changes has also been put forward, all of which show that the effect of gravity is to reduce the velocity of the venous stream in the lower limbs (Waterfield, 1931; Wilburne, 1942; Starr, 1943; Starr and Maycock, 1945; Wilkins *et al.*, 1950). Our observations provide further support for the belief that the flow-rate is greatly decreased when the subject rises. This retardation may well be a potent factor in the onset of syncope that occurs in persons kept standing upright for considerable periods, as with troops on parade. Concurrent with and dependent upon the decrease in flow-rate, the venous pressure in the legs rises (Pollack and Wood, 1949), fluid passes out into the surrounding tissues and œdema develops. At the same time, the failure of venous return from the legs causes a diminution of cardiac output (Brigden *et al.*, 1950) and fainting may occur.

The same effect is observed, though to a lesser degree, in the sitting position with the legs down. Pollack and Wood (1949) showed that the pressure in the saphenous veins rose in both standing and sitting postures, and it is probable that their observations are dependent upon the reduction of flow-rate demonstrated by our method.

Since it has been suggested that pressure behind the knees may be a factor in reducing venous flow-rate, measurements were made in the crossed-knee sitting posture. The subject was asked to cross the knees in the most comfortable and natural manner and to remain for five minutes without moving. The upper (crossed-over) foot, into which the injection was made is not fully dependent in this attitude, and the knee is higher than the groin. The flow-rates recorded were very variable from subject to subject; the average for the group being slightly greater than that for the standard position. Statistically, the difference between the crossed-knee sitting and standard positions was not significant. The pressure exerted behind the knee in this naturally comfortable posture was not great and the effect noted by Simpson (1940), on the importance of such pressure on the incidence of pulmonary embolism, was not reproduced.

The increased rate of flow in the lower limbs that occurs when the body is tipped head downwards was studied in animals by Hill (1895) more than half a century ago and was ascribed by him to the effect of gravity. His observations have been used from time to time as an argument in favour of nursing surgical cases with the foot of the bed raised (Oschner, 1946) for at least a part of the day until the patient is sufficiently recovered to make voluntary muscular contractions of the legs. By elevating the leg from the horizontal position, Kvale *et al.* (1940) demonstrated a decrease of 8–25 per cent in the foot/carotid time and Wilkins *et al.* (1950) reported that, in the head-down position, venous pressure in the feet and legs fell almost to that of the atmosphere. Our flow-rate measurements also have shown that venous velocity is markedly increased when the subject is tipped with the head 10 degrees down; the rate is almost double that found in the horizontal position. In view of this finding, therefore, it appears that the practice of raising the bed foot for short periods in those cases that are immobilized may well be a good prophylactic against the onset of thrombosis, especially in patients where other factors in the pathogenesis of coagulation are minimal. It was previously shown that in bed-ridden surgical patients, a progressive decrease of the venous flow-rate occurred in the lower limbs (Wright *et al.*, 1951), while in those who were ambulatory early in convalescence, no such slowing of the venous stream was demonstrable. Any measure that can increase the rate of blood flow in the legs of patients nursed in bed may, therefore, be of practical value. At the same time Frykholm (1940) has pointed out that to keep the foot of the bed raised for long periods may damage the veins of the leg by allowing the intimal surfaces to come into contact with each other, and thus injure the cells.

The effect of exercise on venous flow has been investigated in various ways. In all reports the rate has been shown to increase with exercise (Thompson *et al.*, 1927; Kvale and Allen, 1939; Kvale *et al.*, 1940; Heller, 1942; Pollack and Wood, 1949; Wilkinson *et al.*, 1950; Gollwitzer-Meier, 1950). The types and degrees of exercise varied from one report to another, as also the method of measuring the change. The present findings, however, of an increased venous flow-rate of between two and three times that in the standard supine position is of the same order of magnitude as those of other observers. It is of interest that such a profound change should be produced by so small a movement as dorsi- and plantar-flexion of the foot and it appears that this simple exercise offers a satisfactory method of ensuring a rapid venous flow-rate in those patients who must be kept recumbent. Even the old and frail, or the seriously ill can be required several times a day to perform the simple " pedalling " movement shown here to be so effective in combating venous stasis.

Summary

Venous velocities, measured by an injection of $^{24}NaCl$, have been shown to be equal in both legs. Day-to-day measurements in normal subjects, under *standard* conditions have been shown to fluctuate by about 25 per cent of the initial flow-rate.

A comparison of venous velocity in the horizontal and various other positions has been made, and figures are given for the mean flow-rates observed. Venous flow-rate is about halved when the subject stands or sits when compared with that in the supine position. Venous flow-rate is doubled when the subject is tipped head-downwards or after vigorous dorsi- and plantar-flexion of the foot.

The significance of these findings is discussed with special reference to the incidence of venous thrombosis.

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THE PRÆCORDIAL T DEFLECTION OF THE ELECTROCARDIOGRAM

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The variations in the behaviour of the T deflection of the human electrocardiogram in the præcordial positions V1–V4 observed in certain experimental and clinical conditions gives some information on the origin and composition of this wave. By relating the anatomical site of muscle involvement with the observed changes in the T wave, objective evidence as to the order of the repolarization process in the human heart can be presented. The clinical significance of different patterns of T wave inversion can be discussed as a result of these observations. An explanation of the possible mechanism underlying T wave inversion can also be attempted.

Inversion of the T wave by Cooling the Præcordium

Cooling the præcordium by means of an ice-bag will produce negativity of T waves previously recorded as positive in the leads reflecting potentials from the heart muscle underlying the cooled area of chest wall V1–V4 (Brink, 1951). The electrocardiograms shown in Fig. 1 were taken before and after cooling the anterior chest wall of a young, healthy man. The following points deserve particular notice.

(1) The time taken for the cooling process to produce this change was approximately 40 minutes. This suggests that the lowering of the temperature on the outer surface of the heart only takes place after the chest wall has been sufficiently cooled to permit such deep penetration of effect. In patients who have thick chest walls, or in whom one may expect that much lung tissue is interposed between the chest wall and the heart, this local effect is increasingly difficult to produce. Thus, young people were found to be more suitable for the demonstration of the cooling effect. After the age of 30, one only rarely manages to show any change in T wave form by cooling.

(2) The change in T wave direction is limited to leads in the frontal plane. The standard leads and unipolar limb leads remain unchanged. This again indicates that the cooling effect produces only a very local change in the cardiac muscle.

(3) In Fig. 1c two complexes taken in the position VB are shown. The first was taken before cooling was commenced ; the second after cooling had been completed. It is seen that as T became negative anteriorly, it gained in voltage posteriorly. Fig. 2 demonstrates the order in which the T wave negativity starts and comes to completion, and the order in which it recovers from the effects of cooling (a and b). The first change to take place can clearly be seen to be an aberration of the terminal portion of the T wave. This end portion then becomes negative, resulting in a biphasic up-down deflection. As cooling is continued the negativity extends to involve earlier portions of the T deflection. The recovery process again illustrates that the end part of the T is the last to regain its former positivity. If we now accept that the effect of cooling is to produce local changes in the heart muscle, these changes must therefore extend inwards from the pericardial

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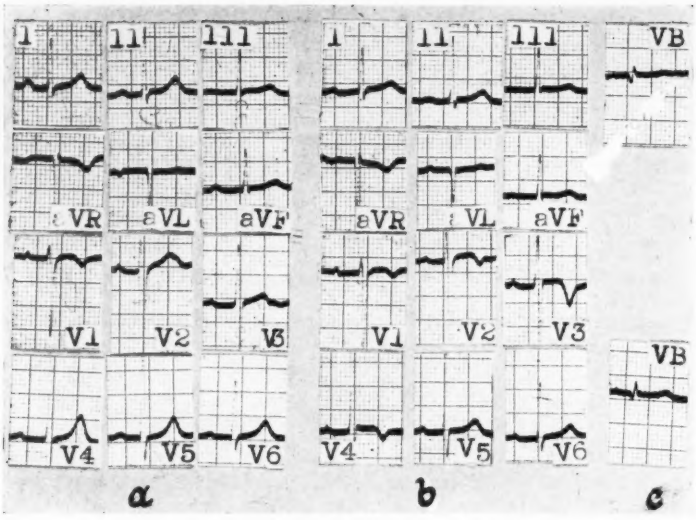

FIG. 1.—Effects of cooling the præcordium by means of an ice bag. (a) Taken before cooling. (b) Taken after cooling for 40 minutes. (c) Lead VB before and after cooling.

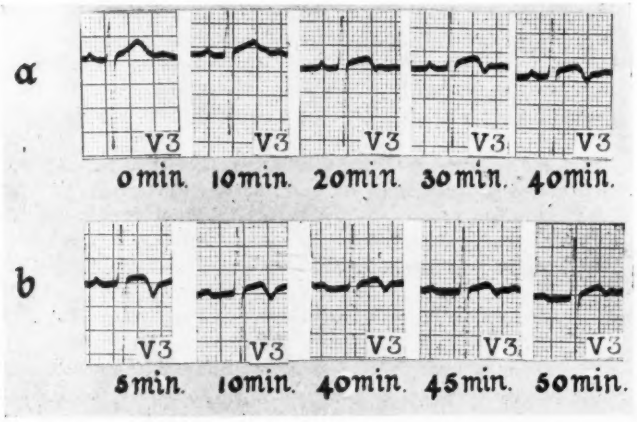

FIG. 2.—Development of electrocardiographic changes resulting from cooling the chest wall. (a) V3 showing progressive T wave inversion, starting in the terminal portion. (b) Progressive T wave recovery ending in the terminal portion.

aspect. Since the end of the T deflection marks the end of the repolarization process in the heart muscle, we must assume that this terminal repolarizing process arises subpericardially, and that the earliest forces of repolarization come from the more deeply situated muscle. This behaviour of the T wave therefore suggests that the wave of recovery begins subendocardially and spreads outward through the heart muscle. It appears to follow the same course, therefore, as does the depolarizing wave. We would therefore have to infer that the first muscle to become active is also the first to recover. This view is not the one more generally held (Ashman and Hull, 1944).

THE CHANGE PRODUCED BY LOCAL MUSCLE DAMAGE

Case 1. In Fig. 3 is shown the electrocardiogram of a man aged 66, taken two weeks after the onset of pain in the chest which first came on after exertion but later occurred also at rest. On admission he had a blood pressure of 150/54. There was no evidence of cardiac failure. He had a normal erythrocyte sedimentation rate (8 mm./hour). He died unexpectedly six weeks after admission. During this time five electrocardiograms showed the pattern to change from that seen in *a* to that in *b*. The terminal T wave inversion remained constant.

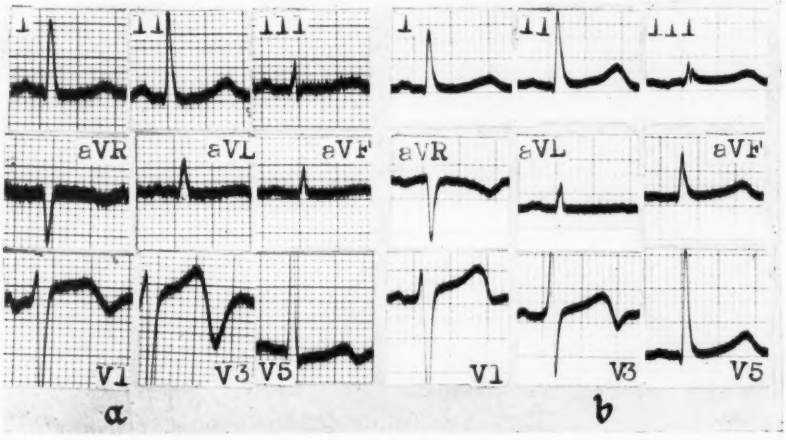

FIG. 3.—Case 1. History of myocardial infarction. (a) Earlier electrocardiographic changes. Deep T inversion V3. (b) Subsequent persistent change. Terminal depression TV3.

Post-mortem findings. No gross infarct was found macroscopically. A microscopic area of fibrosis well localized in the outer third of the anterior left ventricular wall (Fig. 4) was found to be present. In this area muscle fibres can be seen caught up in dense collagen tissue.

Comment. The pattern of terminal T depression in the præcordial lead V3 may therefore be taken to be the only indication of permanent muscle damage in the anterior wall of the heart. The situation of this damaged muscle supports the view that the terminal T arises from the more superficial heart muscle. Although this type of infarct is as liable to produce symptoms and signs, it is from its situation not as likely to cause severe complications such as perforation and endocardial thrombus formation with embolization. For this reason one would not be likely to meet this type of infarct frequently as a fresh one in the autopsy room. The cases that carry a good prognosis and do not require prolonged bed rest and continued anticoagulant therapy may have this type of infarct. Indeed, this type of graph can be seen to correspond very well with some of the published graphs of Papp and Smith (1951) in their discussions on cardiographic patterns in slight coronary attacks.

It would appear from the comparison of the effects of cooling the præcordium and the effects of muscle damage that very little interference may result in extensive T wave changes, and that when T wave effects are the only cardiographic manifestation of muscle damage, the lesion is probably not large, and only superficial. This concept might permit less vigorous treatment.

Case 2. The electrocardiogram shown in Fig. 5a was taken while the patient, a man of 70, attended the out-patient department for angina of effort. This shows only the pattern of left ventricular hypertrophy. Graph (b) was taken two weeks after a severe nocturnal chest pain which had radiated to the throat and both arms. The duration of this pain had been 24 hours.

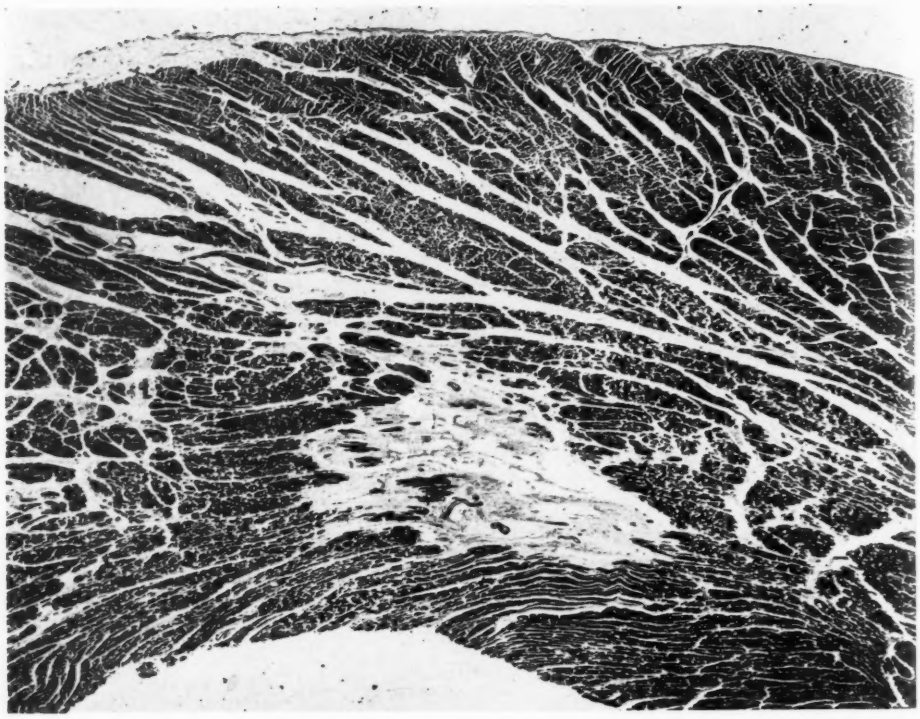

FIG. 4.—Microscopic section from anterior left ventricular wall of Case 1. Localized area of fibrosis. A few muscle fibres seem to be caught up in dense collagen tissue. Situation outer third of ventricular wall.

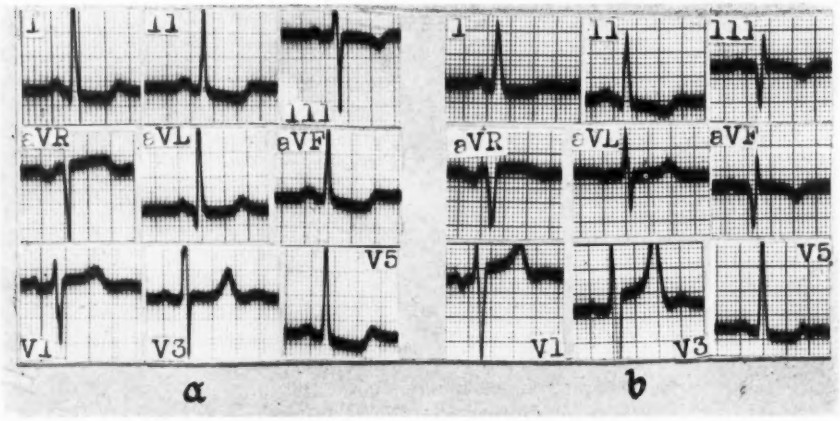

FIG. 5.—Case 2. (a) Pattern of left ventricular hypertrophy. (b) Two weeks after history of myocardial infarction shows a posterior infarction and tall TV3.

The electrocardiogram has now changed remarkably, showing a QIII TIII and a QVF TVF pattern of a posterior myocardial infarct. The T wave in V3 had increased in amplitude from 5 mm. to more than 15 mm.

Comment. In this case the T in the præcordial lead is conspicuously augmented by a lesion in myocardial muscle situated in the heart wall opposite to that which is recorded electrocardiographically in V3.

Case 3. A man, aged 52 years, had episodes of severe substernal pain radiating down both arms into the wrists. They came on at rest and lasted 5 to 10 minutes. After several of these attacks over a period of twelve hours, he developed a more prolonged one which required morphia for relief, and he was then admitted to hospital. The first electrocardiogram taken (Fig. 6a) was

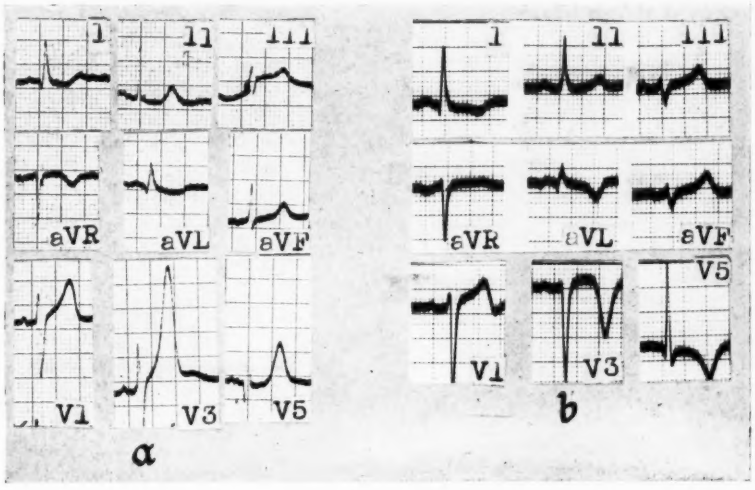

FIG. 6.—Case 3. History of myocardial infarction. (a) 24 hours after onset of symptoms. Tall TV3. (b) 18 days after (a). No further clinical incidents in the interim. Now shows anterior myocardial infarction.

about 24 hours after the onset of these symptoms. The extraordinarily large amplitude of T in the præcordial leads, particularly V3 (27 mm.) was the only noteworthy feature at this stage. The leucocyte count rose to 23,000 per c.mm. The erythrocyte sedimentation rate, at first normal, went up to 52 mm. in one hour after four days. The pain continued for three days, and thereafter there were no further recurrences. The next cardiogram (Fig. 6b) was taken 18 days after the first. The change in the præcordial T is quite obvious and the pattern now clearly resembles that of an extensive anterior infarct.

Comment. The first electrocardiographic effect of this anterior lesion had therefore been an augmentation of the T wave in the præcordial leads. This has previously been recorded (Wood and Wolferth, 1934) and could be interpreted as meaning an initial reactive hyperæmia in the damaged area.

DISCUSSION

Three salient features emerge from the above descriptions of the effect of cooling and of local muscle damage. (1) The evidence produced suggests that the order of repolarization proceeds from the endocardial aspect to the pericardial aspect of the heart. (2) Effects in one region of muscle result in an alteration of the T wave recorded from the opposing muscle mass. (3) When the muscle affected is superficial it is only the terminal T that shows any change.

Individual muscle bundles may therefore influence one another during the process of repolarization and in the formation of the T wave. They influence each other in such a way that opposing

sides of the heart would appear to produce a balance between the forces that go to make the T wave (Fig. 7). If this balance is upset the unaffected side escapes the normal damping effect of the opposite side, as is the case with the tall T in V3 in the posterior infarct (Fig. 5 and Fig. 7c). However, the reactive hyperæmia, which may appear early during a coronary thrombosis, may allow the repolarizing forces to predominate in the affected wall and result first in very tall T waves, as in Fig. 6. Later with ischæmia developing, the anterior wall has less influence than the posterior and the characteristic negative T waves result (Fig. 6).

Since the more superficial myocardial muscle appears to be responsible for the end portion of the T wave, a lesion affecting only these bundles may be expected to produce the terminal T wave inversion as seen in Fig. 3a and b. These patterns are seen to correspond accurately with the changes produced by the process of cooling (Fig. 2).

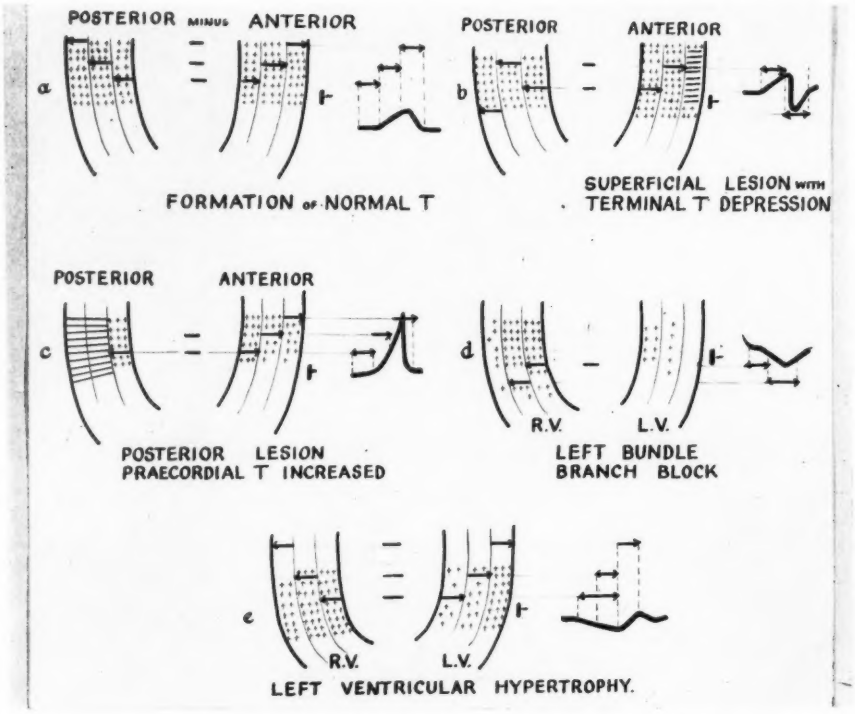

FIG. 7.—Diagrammatic representation of the spread of recovery process. (a) In the formation of normal T wave. (b) In the production of the terminal T depression by superficial lesion. (c) Augmentation of T in V3 by a posterior lesion. (d) Inversion of T in bundle branch block. (e) S–T depression and early T wave inversion in ventricular hypertrophy.

In the same way that activation spreads through the cardiac muscle from endocardial to pericardial aspect, so recovery proceeds in the same direction. Whereas the forces representing activation are rapid, the recovery process is about four times as slow (Craib, 1930). This means that the QRS complex represents the different phases of muscle bundle activation in succession—a march of events—giving rise to the individual deflections and varying according to the site of the electrode. The T wave, however, is formed by the simultaneous contribution of muscle fibres undergoing recovery on all sides of the heart at the same time—a summation of events—and hence

the contour of the T is the same on all pericardial aspects of the heart. Where heart muscle is very close to the electrode, the forces arising here may predominate to such an extent that the T is relatively tallest here and also leaves the base line earlier, resulting in a short S-T segment. This is frequently the case in positions V2 and V3.

The earliest recovery processes are to be expected in the subendocardial regions on all sides of the heart. Since they are spreading away from each other and are relatively far from the recording electrode, they would tend to cancel each other and be recorded as a straight line—the S–T segment (Fig. 7a). When the repolarization approaches more superficial areas it gradually has more and more influence on the recording electrode and the slowly rising limb of the T wave takes place. The T deflection is therefore formed on all sides of the heart by the more peripheral muscle fibres only (Fig. 7a). For this reason probably, one can produce complete negativity of the T by merely cooling the superficial layers of heart muscle. Thus, also, relatively mild ischæmia of superficial areas may be the cause of extensive T wave changes.

The S–T segment and early T deflection must therefore represent the forces of repolarization from subendocardial muscle fibres. When this portion of the electrocardiogram is primarily affected, we may therefore localize the site of the involved muscle in the deeper lying myocardium.

We may apply these principles in the interpretation of the T wave inversion in other conditions (Fig. 7 and 8).

1. *Bundle branch block* (Fig. 7). Here activation proceeds first to the normal side of the heart and hence these fibres will also be the first to start recovery. When the activating process reaches the blocked side and sets off recovery there, the normal ventricle has already a larger number of fibres undergoing repolarization, and will therefore predominate in influence on an electrode recording events from the blocked side with resulting negativity of the T wave.

2. *Ventricular hypertrophy* (Fig. 7). Although the fibres become hypertrophied, their number remains the same. Many of them are relatively ischæmic because the capillary vessels do not multiply (Wearn, 1940). Repolarization forces from the hypertrophied side can therefore become only less in magnitude. This results in repolarizing forces from the normal ventricle, predominating in influence over those from the hypertrophied chamber, and therefore there is initial T wave negativity recorded over the hypertrophied ventricle. In the case of hypertrophy it can be observed that it is the early T which first becomes negative resulting in a biphasic down-up T. This suggests that the deeper lying heart muscle becomes involved at an earlier date than the more superficial.

3. *Digitalis effect*. The changes here consist of a depression of the terminal S–T segment and early T wave with a biphasic down-up deflection. When digitalis effect is seen in cases with left ventricular damage, the changes are almost invariably to be seen in the leads reflecting left ventricular potentials. Reciprocal changes are seen from the right ventricle. Judged electrocardiographically, digitalis seems to affect the more severely damaged fibres most, that is to say, those situated subendocardially and in the ventricle which is under stress. This is in accordance with the generally accepted view that digitalis has a greater effect on pathological material.

4. *The inverted præcordial T wave of normal children* (Fig. 8a and b). In a series of 53 normal children between the ages of 16 months and 15 years, T was inverted in præcordial leads as far as V4 in 5 cases. On inspecting the pattern of T wave negativity in those cases where this deflection is not completely negative but biphasic it was found that the terminal T tended to be positive (Fig. 8b). This suggests that the last portion of heart muscle to recover and hence the last portion to become active, is the area underlying the electrode in positions V1 to V4. This is right ventricular muscle and it appears then that the T wave inversion may be explained by a degree of physiological right ventricular block.

5. *The normally occurring inverted T wave in adult Negro and South African Bantu.* In a series of 100 normal adults from the Bantu races, 50 men and 50 women, ranging in age from 18 years to 50 years, the T deflection was found to be negative as far as V4 in 4 cases. Where these deflections are incompletely negative they show a biphasic pattern with depression of the terminal portion

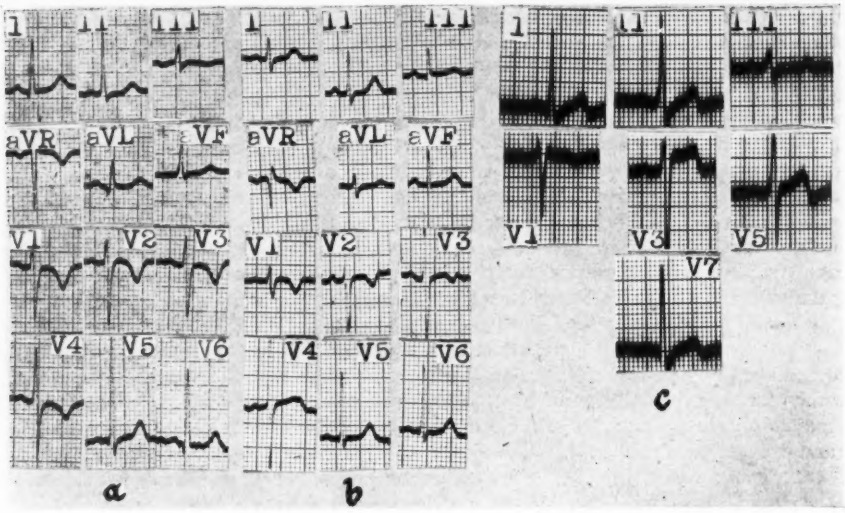

FIG. 8.—T wave inversion in the præcordial leads of normal children and adults of the Bantu race. (a) Child, aged 11 years. T negative V1 to V4. (b) Child, aged 7 years. Terminal portion of T position in V3. (c) Adult Bantu, aged 25 years. Terminal T negative in V3.

(Fig. 8c). This pattern contrasts with that found in normal children and it would appear that in the adult Bantu the negative præcordial T wave cannot be ascribed to a persistence of the juvenile pattern. Here the explanation may rest either with some mechanical influence of the anterior chest wall on the heart surface, or with greater repolarizing forces posteriorly. Increased blood supply may result in increase of the magnitude of the recovery forces as with the reactive hyperæmia (Fig. 6). The posterior wall of the Bantu heart is thought to be more richly endowed with blood vessels than in European races (Brink, 1949), and hence this may on accasion be sufficient reason for the negative præcordial T wave.

SUMMARY

The T wave in position V1 to V4 may be inverted by prolonged cooling of the anterior chest wall. The order in which this inversion takes place suggests that repolarization follows the same path as depolarization, namely, from within out. Small superficial areas of muscle damage in the anterior wall are shown to produce effects comparable to the cooling procedure.

T wave changes as the only indication of muscle damage are thought to represent only a superficial lesion. Such a lesion may not require a vigorous regime of treatment. Terminal T wave depression may be the only evidence of permanent muscle damage.

An analysis and interpretation is attempted of the formation of the normal T wave and inversion occurring in such conditions as bundle branch block, ventricular hypertrophy, and digitalis effect, and in normal children and the adult Negro and Bantu.

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THE VECTORCARDIOGRAM OF CARDIAC INFARCTION

BY

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A simple method of drawing the three-plane projection of the spatial vectorcardiogram has been described (Shillingford and Brigden, 1951). A series of normal vectorcardiograms were studied and found to have certain constant characteristics that were comparable with the results obtained by electronic methods. In this paper we report the vectorcardiographic findings of extensive cardiac infarction, and the abnormal patterns obtained have been related to the QRS–T complexes recorded from the same patients in the conventional manner. Duchosal and Sulzer (1949) and Vastesaeger (1949) have studied the vectorcardiogram of cardiac infarction, using an electronic apparatus. Our findings are in substantial agreement with those recently reported by Scherlis and Grishman (1951); their three-plane vectorcardiograms were seen simultaneously on a tribeam cathode-ray tube and photographed on one film.

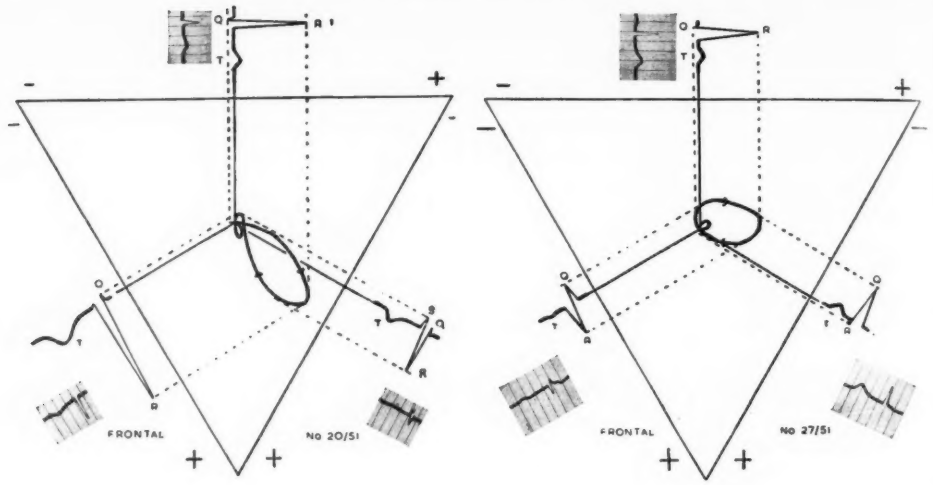
METHOD

The method of integrating the scalar electrocardiograms has been the same as we described, but the lead positions of the reference system have been slightly modified. The voltage obtained from leads in the horizontal plane in the system advocated by Duchosal and Sulzer (1949) is small, and it was found that the higher voltage that could be obtained by bringing the electrodes nearer to the heart, made the vectorcardiogram easier to correlate with the conventional chest leads. The horizontal lead positions have therefore been raised from the iliac spine level to a plane through the xiphisternum; the reference system then becomes almost cuboidal. It is appreciated that there are certain theoretical objections to placing electrodes any nearer the heart, but this new position is considered to be a reasonable compromise that sacrifices little fundamental accuracy and facilitates interpretation of the loop. Grishman *et al.* (1951) have made similar changes in the lead positions.

The validity of this method is shown by the similarities of the QRS complexes reconstructed from our vectorcardiograms and the actual leads obtained by the conventional method. In Fig. 1A the reconstructed QRS complexes from the frontal plane loop are compared with the standard leads recorded from the same normal subject. A reconstruction of the unipolar chest leads from the horizontal plane loop is shown in Fig. 2A together with the recorded unipolar chest leads. The projections in three planes of the spatial vectorcardiogram have been drawn in 20 cases of cardiac infarction, of which 10 were anterior and 10 posterior in position. All observations were made with the subject in a reclining position. Each patient had a history of prolonged chest pain at rest, and an electrocardiogram that showed pathological Q waves.

RESULTS

Four examples of the vectorcardiogram in patients with posterior cardiac infarction are shown in Fig. 3, and a frontal projection is shown with the reconstructed complexes alongside the recorded limb leads in Fig. 1B. All the patients with this condition showed loops that were initially directed upwards in the frontal plane and tended to lie in the upper quadrants; the sagittal view (Fig. 3) of the loop shows the same upwards deviation. The horizontal projection showed no constant



A B

FIG. 1.—(A) The frontal projection of a normal vectorcardiogram with reconstruction of leads I, II, and III, and with actual recordings for comparison. (B) The frontal plane vectorcardiogram of a case of posterior cardiac infarction. A deep QII and QIII are associated with the upward shift of this loop.

abnormality, but in one case (Fig. 3, No. 1) there was a forward shift of the whole loop and in another (Fig. 3, No. 2) there was a forward indentation of the returning limb with a corresponding forward bulge of the outgoing limb. These abnormalities are believed to be due to an area of posterolateral infarction in addition to the area of inferior infarction. It will be seen (Fig. 1B) that this abnormal deviation of the cardiac vectors into the upper quadrants results in the appearance of Q waves in the reconstruction of leads II and III. The time taken for the inscription of the QRS loop was within normal limits, while its direction of rotation was not constant. The T loop was found to be directed upwards in the frontal plane, and there was little change in the horizontal plane.

Four examples of the vectorcardiogram in patients with anterior cardiac infarction are shown in Fig. 4, and the horizontal loop from one patient is shown in Fig. 2B with reconstructed chest leads alongside the unipolar chest leads 1, 4, and 7. In this group the QRS loop has shifted backwards in the chest, a change that can be seen both in the horizontal and sagittal projections. In the sagittal view neither the outgoing nor returning limb of the loop projects into the anterior quadrants, i.e. to the right of the vertical isoelectric line. This backwards shift of the QRS vectors results in the appearance of Q waves in reconstructed anterior chest leads. The absence of any vectors in front of the isoelectric line in the sagittal view similarly is a reflection of the Q waves found in the centre of the chest in anterior cardiac infarction. The time taken for the inscription of the QRS was within normal limits and the direction of the rotation of the loop was not constant. The T loop was found to be directed backwards and to the left, i.e. in the same direction as the QRS loop, but in the case of an old cardiac infarction the T loop was orientated in the normal way (Fig. 4, No. 2, 3, and 4).

It has been shown that when due allowances are made for the distance of the electrodes from the centre of the heart, tracings are obtained at opposite points on the surface of the chest that are mirror images (Duchosal, 1951). It was expected, therefore, that the retreat of the vector loop from the site of the infarction would result in the appearance of R waves in leads taken diametrically opposite to those showing Q waves. This effect is well shown in a patient with anterior cardiac

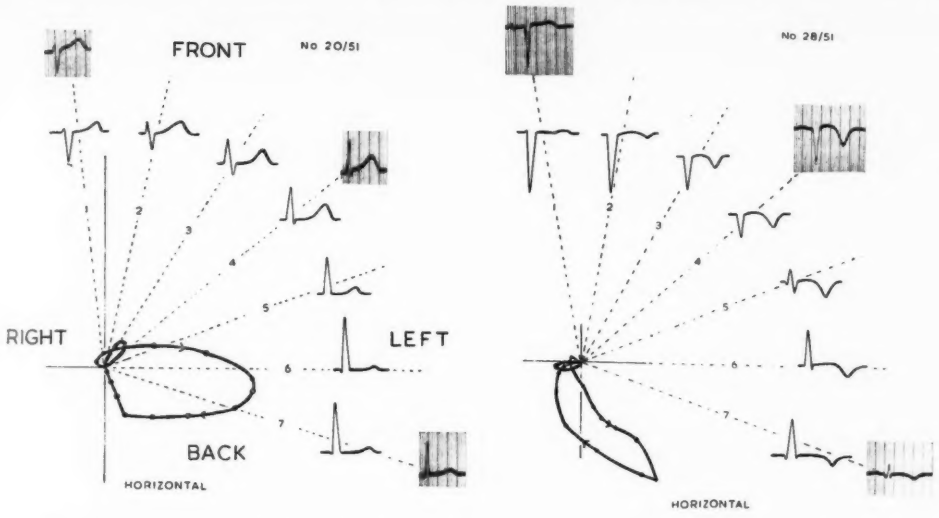


FIG. 2.—(A) The horizontal projection of a normal vectorcardiogram showing reconstructed chest leads and leads V1, V4, and V7. (B) A similar projection in anterior cardiac infarction. Deep "Q waves" appear in the reconstructed QRS complexes due to backward shift of the loop. The leads V1, V4, and V7 are in the appropriate positions.

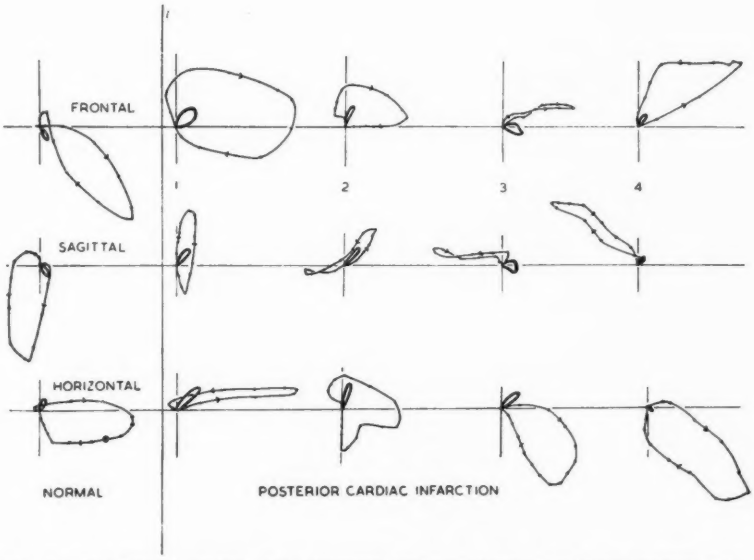


FIG. 3.—The frontal, sagittal, and horizontal vectorcardiograms of four patients with posterior cardiac infarction, for comparison with the normal.

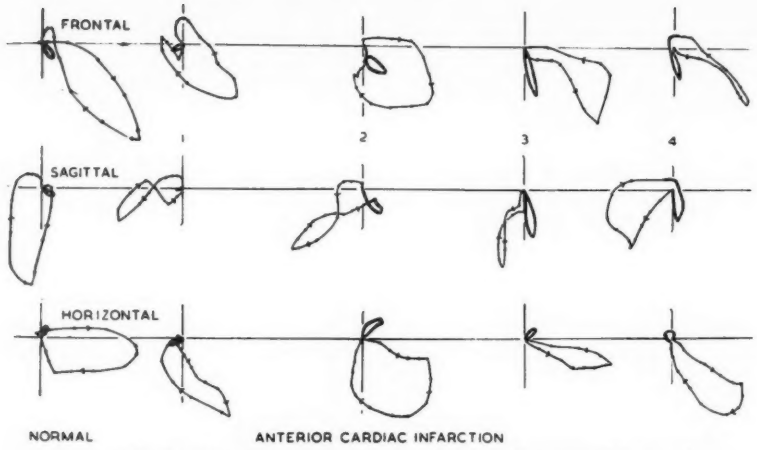


FIG. 4.—The frontal, sagittal, and horizontal vectorcardiograms of four patients with anterior cardiac infarction.

infarction on whom 12 unipolar leads were taken round the chest and correlated with the horizontal projection of the vectorcardiogram (Fig. 5).

DISCUSSION

All the patients chosen for this study had evidence of cardiac infarction with pathological Q waves in the electrocardiogram. The vectorcardiogram of all showed a characteristic shift of the loop away from the unipolar leads recording Q waves. This is readily seen in the horizontal loop of anterior cardiac infarction as is shown in Fig. 2B. The reorientation of the loop away from the lead positions that show Q waves is also seen in the case of posterior infarction for here the relevant unipolar lead with Q waves is VF, the axis of which is a line approximately bisecting the apex of Einthoven's triangle, and the loop in this case has moved away from the apex towards the base of the triangle.

It has frequently been shown in studies relating the electrocardiogram to morbid anatomy that Q waves are found in leads anatomically related to the site of infarction. It therefore follows that the loop of cardiac vectors retreats from the area of infarction; thus, in anterior lesions it shifts backwards in the chest, and in posterior (or better inferior) myocardial infarction, the loop shifts in a cephalad direction. This retreat from the infarcted area (i.e. from leads showing Q waves) inevitably results in the appearance of R waves in leads situated at opposite points on the surface. In cases of anterior infarction, therefore, R waves are found at the back of the chest, although such positive waves are of small voltage owing to the increased distance of the electrodes from the heart. In cases of posterior infarction, this shift of the positive vectors into the upper quadrants results in the appearance of positivity in the basal unipolar leads which may be seen in the frequent occurrence of a primary R wave in VR. The appearance of a prominent R wave in lead V1 in cases of lateral myocardial infarction as described by Levy *et al.* (1950) is a similar manifestation of the preponderance of cardiac vectors away from this site of infarction. This change is well shown in the horizontal loop of Fig. 3, No. 2, where the forward bulge of the loop would produce a prominent R in V1.

This constant shift of cardiac vectors away from the damaged area is presumably caused by the preponderant effect of the remaining normal muscle. The Q wave may be seen to represent a recession of the QRS loop away from the site of infarction rather than a transmission of negativity

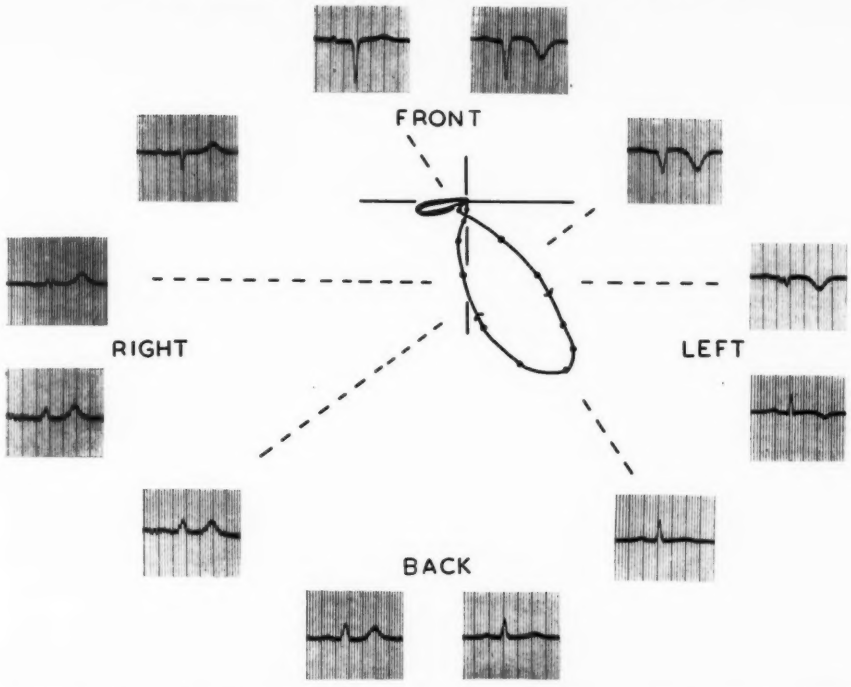


FIG. 5.—The horizontal projection of a vectorcardiogram of anterior cardiac infarction. The loop is characteristically deviated backwards with resultant Q waves in conventional chest lead positions V1, V2, V4, and V6. QRS complex in leads at the back of chest show R waves and upright T waves. The mirror image effect may be observed in most pairs of leads.

from the cavity. This difference in concept depends rather on the investigator's attitude to the subject than a fundamental biophysical difference. However, it may be seen that the vector loop directs the attention to the extent and site of normal muscle as well as to the infarcted area of myocardium.

The changes in the T loop are similar to those of the QRS but the usual " recovery of T waves " is seen in some cases in the return of the T loop to its normal orientation in the chest.

It is not suggested that the methods described add anything to the diagnosis of cardiac infarction for the site and severity of this condition can be assessed by clinical and the more orthodox electrocardiographic methods, but a knowledge of the vectorcardiogram in gross infarction provides a more unified picture of the abnormal electrical activity of the heart as a whole.

SUMMARY

Theoretical QRS–T complexes have been reconstructed from the frontal and horizontal plane projections of the spatial vectorcardiogram and shown to resemble closely those obtained by conventional electrocardiography. Three plane projections of the vectorcardiogram have been drawn in 20 cases of cardiac infarction.

The vectorcardiogram of anterior cardiac infarction shows a constant deviation of the loop from the site of infarction: this is best seen in the horizontal plane. A similar deviation of the

loop away from the site of infarction is seen in cases of posterior infarction, and is shown best in the frontal plane.

The significance of these findings has been discussed in relation to the appearance of pathological waves in the conventional surface leads.

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PERSISTENT ECTOPIC AURICULAR TACHYCARDIA IN CHILDREN

BY

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Paroxysmal tachycardia is not uncommon in infancy and early childhood. The paroxysms are usually of short duration and may be characterized by attacks of abdominal pain and vomiting, sometimes associated with collapse (Hubbard, 1941). Prolonged attacks in children have been reported by Parkinson and Papp (1947) and by Miller and Perelman (1945).

Three further cases of prolonged tachycardia are described in this paper. They are of interest because in one there was no evidence of a normal sino-auricular node and in two there appeared to be two ectopic foci; in none of the three did persistent tachycardia at a high rate over a long period lead to the development of cardiac failure.

Case 1. Ann W., aged 6 years, was first seen when 14 months, because of a rapid heart rate which had been noted by her family doctor for the first time at 6 months of age. She was symptomless.

Examination showed a regular pulse rate of 180 a minute, a very soft systolic murmur audible down the left border of the sternum, and radiological evidence of slight cardiac enlargement involving especially the conus of the right ventricle. An electrocardiogram showed an ectopic auricular tachycardia of 200 a minute with inverted P waves in leads II and III (Fig. 1). At 16 months of age an unsuccessful attempt was made to establish normal rhythm by the successive exhibition of digoxin, strophanthin, and quinidine sulphate.

During the next four years she remained symptomless. The tachycardia persisted, although at a slightly lower rate, and cardiograms showed no change. At 6 years of age a further attempt was made to establish normal rhythm. Digoxin was given orally, an initial daily dose of 0·25 mg. being increased gradually until she was taking 0·82 mg. daily which was maintained for 18 days without symptoms of toxicity. Normal complexes appeared in the electrocardiogram for the first time on the second day of treatment. By the fourth day periods of normal rhythm at about 60 a minute were alternating with the ectopic rhythm at 140 a minute (Fig. 2). The beats at the slower rate showed upright P waves in lead II and some biphasic and some negative P waves in lead III; slight S–T depression was also present. At the end of 43 days treatment normal rhythm appeared to be well established with no further ectopic beats and no S–T depression. The dose was then gradually reduced until digoxin was discontinued altogether after 88 days of treatment during which she had taken a total of 48 mg.

Within one week of complete withdrawal of the drug, paroxysms of the ectopic rhythm were again observed. Digoxin was, therefore, restarted and it has been found that 0·5 mg. daily will maintain normal rhythm (Fig. 3) while with a smaller dose the ectopic rhythm tends to recur.

Case 2, Mary M., aged 3½ years, was first seen with a history of recurring attacks of abdominal pain and vomiting for three months. Physical examination on this occasion showed no abnormality, but when seen again three weeks later she was having a further attack. The pulse rate was then found to be 200 a minute. She was pale and slightly cyanosed with raised jugular venous pressure and enlargement of the liver; there was no œdema or congestion of the lungs. The apex beat was in the fifth space, three and a half inches from the mid-line; the heart sounds were normal and no

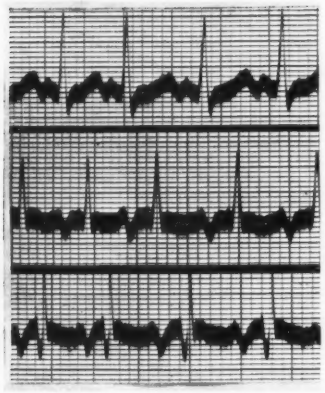

FIG. 1.—Case 1 (21/2/47), aged 14 months. Ectopic auricular tachycardia. Rate 200 a minute.

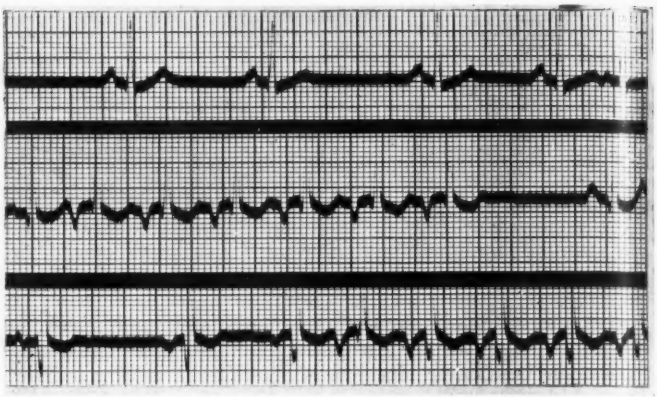

FIG. 2.—Case 1 (23/2/51), aged 6 years. During digitalization. Periods of normal S-A rhythm and of ectopic auricular rhythm.

murmurs were detected. The heart rate was not affected by carotid sinus pressure or by an injection of prostigmine (0·5 mg.).

The cardiogram (Fig. 4) showed auriculoventricular nodal tachycardia at a rate of 270 a minute. Digoxin was given by mouth in doses of 0·25 mg. 6-hourly. Within 24 hours the pulse rate had fallen to 80 a minute and there were frequent premature beats. After 48 hours the pulse rate was 50 a minute and there were coupled beats at the apex. A cardiogram (Fig. 5) at 72 hours showed an auricular tachycardia of 180 a minute with prolongation of the P–R interval and a 2:1 auriculoventricular block. Digoxin was then discontinued. For a short time after this the pulse was quite irregular, but during the rest of her stay in hospital it remained regular at a rate of 120 a minute.

The signs of cardiac failure disappeared as the pulse rate fell and she had no recurrence of abdominal pain while under observation. The apex beat remained outside the nipple line, the sounds were normal and there were no murmurs.

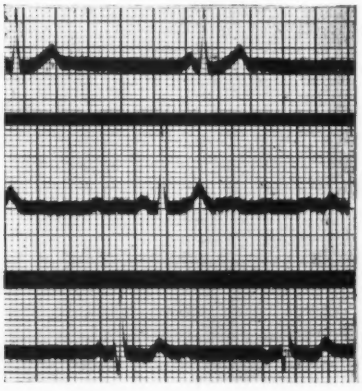

FIG. 3.—Case 1 (5/6/51). Fully digitalized. Normal S-A rhythm.

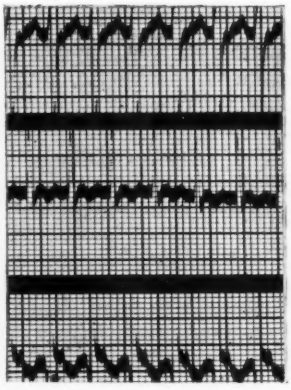

FIG. 4.—Case 2 (3/10/50). Supraventricular (A-V nodal) tachycardia.

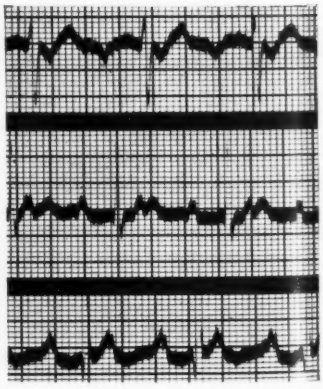

FIG. 5.—Case 2 (6/10/50). Auricular tachycardia. 2:1 auriculoventricular response; inverted P waves; prolonged P–R interval.

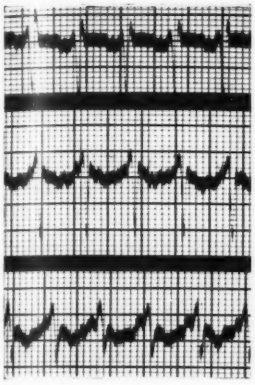

FIG. 6.—Case 2 (3/11/50). During carotid sinus pressure. P waves upright in first two complexes, subsequently inverted.

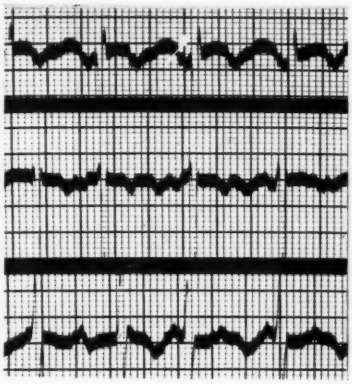

FIG. 7.—Case 2 (25/5/51). Auricular tachycardia. 2:1 auriculo-ventricular responses; occasional supraventricular extrasystoles.

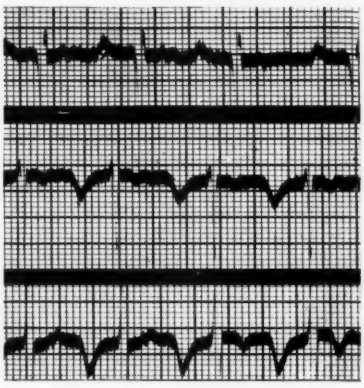

FIG. 8.—Case 3 (19/5/50). Supraventricular (A-V nodal) tachycardia.

A cardiogram one month after admission showed persisting inversion of the P wave in lead 1 with a 1:1 ventricular response and a normal P–R interval. Carotid sinus pressure temporarily restored the P wave to normal but it inverted again while the pressure was still being applied (Fig. 6). She remained quite free from symptoms over the next few months and no treatment was given. The pulse remained regular at a rate of 150 a minute.

Seven months after her first attendance she had another attack of abdominal pain and vomiting and her mother noticed that her heart was beating rapidly. She was seen by her family doctor two days later and was given digoxin 0·25 mg. b.i.d. by mouth. When seen by one of us, two days later, the symptoms had subsided. She looked well and was very active and there were no signs of cardiac failure. The pulse rate was about 100 a minute with frequent premature beats. A cardiogram (Fig. 7) showed an auricular rate of 240 a minute, a 2:1 ventricular response, and occasional supraventricular extrasystoles. The P waves remained abnormal in shape and direction.

Case 3., Alan L., aged 11 years, was admitted to hospital with a history of " shivering " for 9 days and abdominal pain and vomiting for 4 days. Eighteen months previously he had been in hospital with tuberculous osteitis of the right femur. The pulse rate was only recorded for a short period and was then said to be normal.

At 6 years of age he had been attended by his family doctor for acute bronchitis and his mother had been told that he had a " damaged heart."

On admission to hospital he appeared pale but not acutely ill and there were no signs of cardiac failure. The radial pulse was difficult to feel but the rate was about 180 a minute and the rhythm regular. The systolic blood pressure was 105 mm. Hg; the diastolic could not be measured. The apex beat was not displaced, the sounds were normal, and there were no murmurs. The ventricular rate was about 200 a minute. It was not affected by pressure on the carotid sinuses or on the eyeballs; both Valsalva's and Müller's manœuvres and changes of posture were without effect. A cardiogram (Fig. 8) showed auriculo-ventricular nodal tachycardia.

Quinidine by mouth had no effect but a short course of digoxin did slow the heart rate by producing a 2:1 auriculo-ventricular block (Fig. 9). The cardiogram also showed that the tachycardia had now become auricular rather than nodal in origin. A further course of digoxin was given one month later, but as an effective dose caused nausea and vomiting together with the appearance of frequent ventricular extrasystoles (Fig. 10) treatment was abandoned. Subsequent records have

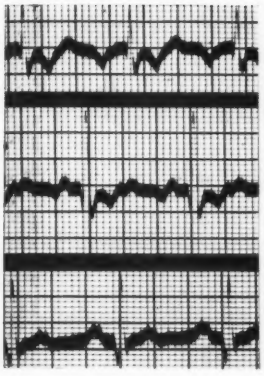

FIG. 9.—Case 3 (31/5/50). Auricular tachycardia with 2 : 1 ventricular response.

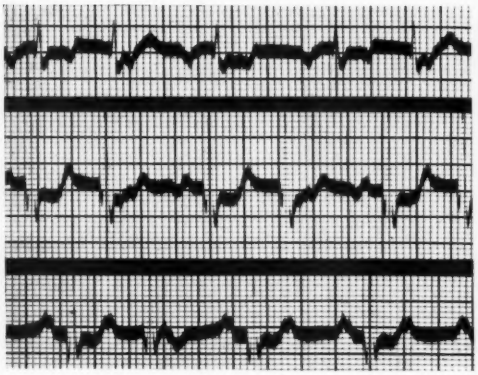

FIG. 10.—Case 3 (18/6/50). Auricular tachycardia with varying degree of A-V block and ventricular extrasystoles.

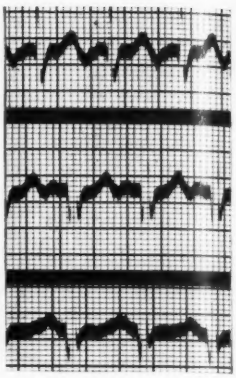

FIG. 11.—Case 3 (25/5/51). Auricular tachycardia with 1 : 1 ventricular response.

shown a regular tachycardia with 1:1 rhythm and persistent inversion of the P waves in lead 1 (Fig. 11).

He received further treatment for the tuberculous osteitis of the femur and was eventually discharged with a walking calliper. During the last ten months he has otherwise been well with no symptoms of cardiac failure and the pulse rate has remained at about 150 a minute.

DISCUSSION

The main point of interest in these three cases is the persistence of an auricular ectopic tachycardia at a high rate over a prolonged period without the development of cardiac failure. Campbell (1947) states that nothing corresponding to established tachycardia has been described but two of these cases are very suggestive of such a condition.

In most instances of prolonged tachycardia that have been reported cardiac failure has developed at some time during the attacks (Maddox, 1937; Miller and Perelman, 1945; Herson and Willington, 1947; and Claiborne, 1950). On the other hand several cases have been described in which cardiac failure did not develop after periods of tachycardia varying from 3 to 43 years (Miller and Perelman, 1945; Weiss and McGuire, 1936).

In Case 1 an auricular tachycardia of 200 a minute was first observed at 14 months and subsequent observation during the next five years showed an average rate of about 160 a minute: cardiac failure did not occur. In Case 2 an auricular tachycardia of 120 a minute persisted for seven months without cardiac failure developing. A short paroxysm of auriculo-ventricular nodal tachycardia at 200 a minute did, however, lead to failure. In Case 3 the ectopic auricular rate has varied from 150 to 180 a minute and there has never been any evidence of cardiac failure.

The absence of cardiac failure during very prolonged periods of marked tachycardia in our cases may be regarded as supporting the contention of Weiss and McGuire (1936) that high cardiac rates up to 150 a minute are not necessarily dangerous provided the heart is otherwise normal. The early evidence of cardiac enlargement in Case 1 may indicate, however, an adverse effect of the tachycardia. On the other hand the enlargement may be due to a congenital cardiac lesion of which there is no other evidence.

In Case 3 another point of interest is the lack of any evidence of the existence of a normal sino-auricular node. In nearly all the published cases, except that of Alimurung *et al.* (1950), normal sino-auricular rhythm has been known to be present before the onset of the paroxysm or has been

demonstrated after the attack. In a few cases where a patient died during an attack or the attack was of long duration the only evidence of the existence of the node was the occurrence of occasional normal sino-auricular beats (Miller and Perelman, 1945). In some cases where a rapid ectopic rhythm was associated with the sudden onset of cardiac failure, it has been assumed that, prior to the attack, slower, normal rhythm was arising in the sino-auricular node although there was no definite evidence of this.

In Case 3 the cardiac rhythm was originating from the auriculo-ventricular node when he was first seen and later appeared to arise from an ectopic auricular focus: there has never been any evidence of a normal sino-auricular node. It is impossible to say how long the abnormal rhythm has been present but the reference to a "damaged heart" five years earlier suggests that it may have been present at that time. In Case 2 there is evidence that a normal sino-auricular node is present as the one record that was obtained during carotid sinus pressure does show normal P waves. However, during the whole of the period she has been under observation, this is the only time they have been shown. During the paroxysm of tachycardia that was recorded the rhythm arose in the auriculo-ventricular node; subsequently it transferred to an ectopic auricular focus where it has persisted. In Case 1 digitalization demonstrated the presence of a normal sino-auricular node but it seems possible that this node had never initiated the cardiac cycle prior to treatment.

Summary

Three cases of persistent ectopic auricular tachycardia in children are described. In one case there was no evidence of the existence of a normal sino-auricular node. In none of the three cases did persistent tachycardia at a high rate over a long period lead to the development of cardiac failure, though in one there were some signs of failure when the rate was unusually fast.

We wish to thank Sir John Parkinson and Professor John Hay for their help in the preparation of this paper, and Professor N. B. Capon and Dr. F. P. Hudson for allowing us access to Cases 2 and 3. We also wish to express our appreciation of the enthusiasm and skill displayed by Messrs. E. J. Caldwell and W. E. Lake in obtaining the electrocardiograms.

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PAROXYSMAL VENTRICULAR STANDSTILL

BY

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Among the various rhythms reported in the course of a Stokes-Adams attack, one of the rarest is standstill of the ventricle as an episode during normal rhythm. Such a condition may be called paroxysmal ventricular standstill, and is to be distinguished from the condition of alternating complete block and normal rhythm to which the term paroxysmal heart block may be applied. Three cases of paroxysmal ventricular standstill have been observed, in two of which there was paroxysmal heart block also, and ventricular standstill was also provoked by carotid sinus pressure.

Weiss and Baker (1933) described several cases of total cardiac standstill, auricular standstlil, or extreme sinus bradycardia, and one of complete block in auricular fibrillation as a result of carotid sinus pressure: all of these had cardiovascular disease. Starling (1921) reported ventricular standstill on swallowing but no cardiographic records were made of the attacks. Yater and Williams (1928–29) described a case of complete cardiac and ventricular standstill with slow irregular P waves. The case of Lewis (1920) showed ventricular standstill with auricular rhythm preserved; this patient later developed a complete block. A case recorded by Alexander and Bauerlein (1936) had variations in the degree of heart block with changes of posture but not with carotid sinus pressure. Holmes and Weill (1945) recorded mild grades of heart block in healthy men when they lay down; carotid sinus pressure caused a decrease in the P–R interval. Turner (1948) recorded the case of a man of 61 with cardiac asystole with pressure on either carotid sinus, whose attacks ceased after bilateral carotid sinus denervation. Parkinson *et. al.* (1941) recorded 5 examples of ventricular standstill, and collected 28 others that had been reported. Among all these there was only one in which the standstill was immediately followed by normal rhythm with unimpaired A-V conduction; this patient showed complete heart block on another day. Isolated cases of ventricular standstill are mentioned in two or three textbooks.

Case Reports

Three patients have been observed with attacks of ventricular standstill, two of whom had normal rhythm and conduction before and after the standstill. In two of them the attacks could be provoked in various ways, in addition to those that had no apparent provocation.

Case 1. A woman of 82 had retinal hæmorrhage and diabetes for which she was having an injection of 50 units of insulin daily. For seven months she had been having syncopal and convulsive attacks. Physical examination was normal except for the retinal hæmorrhage. A cardiogram showed normal rhythm, right bundle branch block, but no delay in A-V conduction. As the record was being completed with lead IV R, the ventricle suddenly stopped with immediate loss of consciousness and a generalized convulsion after 5 seconds (Fig. 1); the movement of the record off the paper indicates the beginning of limb movements. The recording, when resumed at the end of the convulsion shows normal rhythm and conduction exactly as before except that the rate was slightly quicker. As weeks might elapse between this patient's attacks, it was most fortunate that one occurred during the only tracing taken. No further information about the subsequent history was available except that she died a few months later.

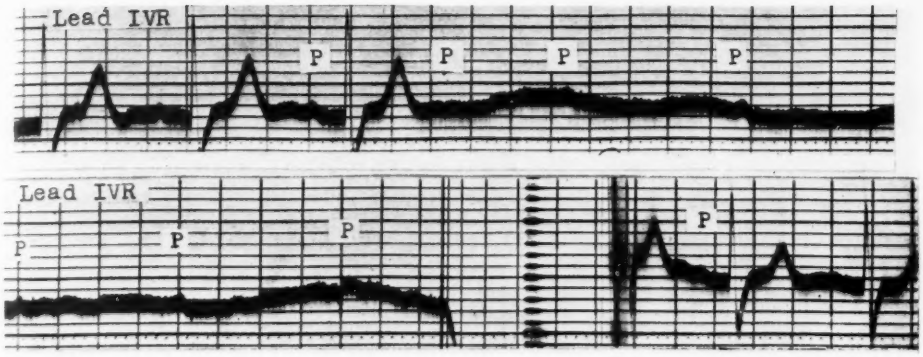

FIG. 1.—Case 1. Woman, aged 82. Spontaneous ventricular standstill; generalized convulsion 5 seconds after the ventricle stops; at end of attack ventricular beating resumed with normal P–R interval.

Case 2. A man, aged 78, with a history of rheumatic fever in childhood and of an illness diagnosed as endocarditis when aged 51, gave a history of " black-outs " for ten years, but only at very long intervals for the first nine years. He developed a gastric ulcer at the age of 77 at which time his syncopal attacks became more frequent. At the apex there was an extra heart sound due to the latent block, but otherwise there was no sign of cardiovascular disease. Normal rhythm with prolonged A-V conduction was usually present (Fig. 2) but sometimes partial or complete

FIG. 2.—Case 2. Man, aged 78. Normal rhythm; P–R interval about 0·3 sec.

heart block. An attack of unconsciousness with convulsion was witnessed in which the peripheral pulse disappeared. Normal rhythm was recorded before and after it. Then very light pressure on the right carotid sinus produced an increase in A-V conduction time for one cycle (Fig. 3) and then ventricular standstill; the auricular rate gradually increased from 65 to 90 a minute, and after about 8 seconds, convulsive movements of the limbs were large enough to jerk the recording pen off the paper. After a few seconds, ventricular activity returned with a rate of about 90, the A-V conduction time being about 0·3 sec., the same as before the attack. Ventricular contractions returned some time before consciousness was fully regained and before limb movements ceased. On other occasions heavy and prolonged carotid sinus pressure would cause only one or two dropped beats with very slight auricular slowing (Fig. 4). This figure also shows a record taken while the patient turned his head vigorously from side to side; it coincided with an auricular extrasystole which was blocked. On yet another occasion when left carotid sinus pressure was without effect, pressure on the right one caused an extreme sinus bradycardia with ventricular escape (Fig. 5). After a ventricular extrasystole, sinus beating was resumed at almost the usual rate in spite of carotid sinus pressure being maintained. When complete block was present, carotid sinus stimulation seemed to be without any effect. Fig. 6 shows complete block with an occasional conducted beat; this last occurs when P falls about 0·3 sec. before QRS. Then pressure on both carotid sinuses successively was exerted; the middle tracing shows the independent

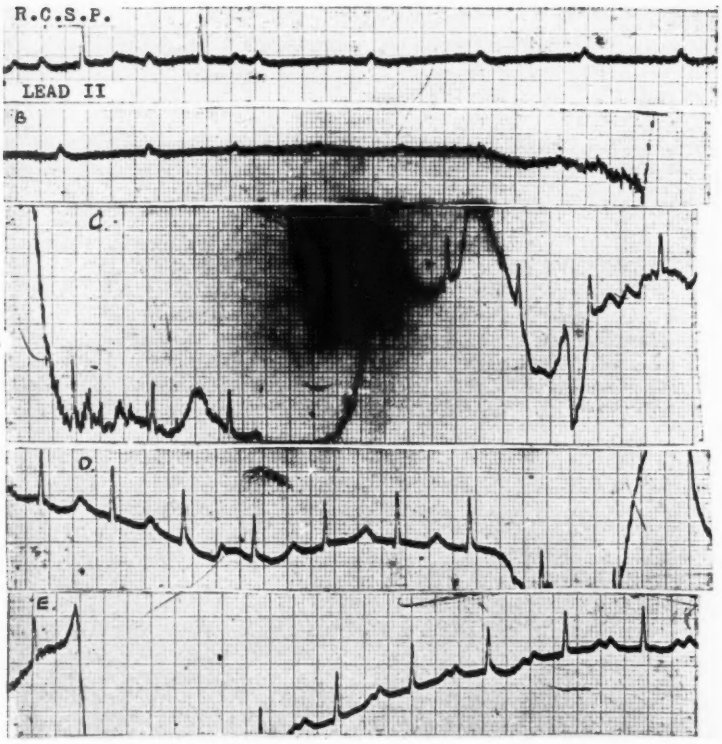

FIG. 3.—Case 2. Light pressure on the right carotid sinus causes increase in the P–R interval for one cycle and then ventricular standstill, leading to convulsion after 8 seconds; a few seconds later A-V rhythm returns with the P–R interval the same as before the attack.

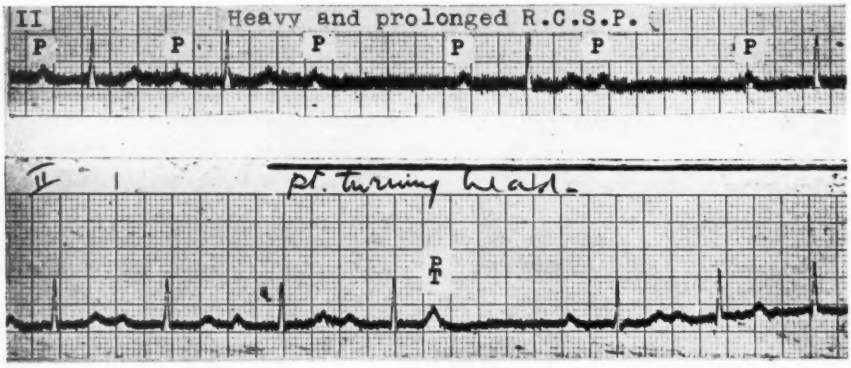

FIG. 4.—Case 2. Upper tracing: heavy and prolonged right carotid sinus pressure caused only one or two dropped beats. Lower tracing: vigorous head-turning by the patient coincided with a blocked auricular extrasystole.

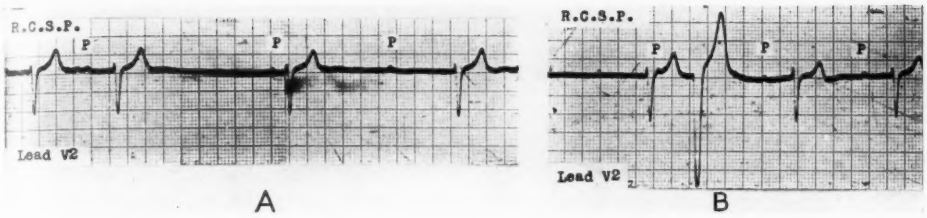

FIG. 5.—Case 2. (A) Right carotid sinus pressure caused sinus bradycardia and ventricular escape. (B) After a ventricular extrasystole, normal rhythm and rate return in spite of continued right carotid sinus pressure.

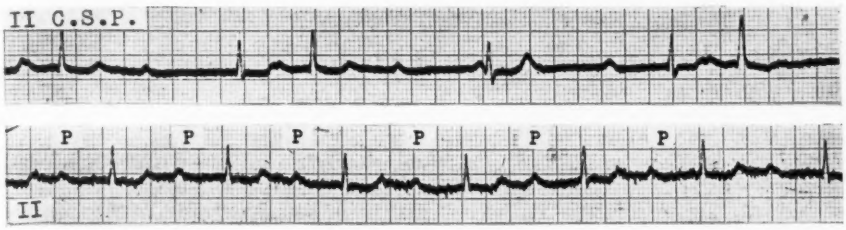

FIG. 6.—Case 2. Upper tracing: complete heart block with occasional A-V conduction; carotid sinus pressure either left or right has no effect. Lower tracing: return of normal rhythm, P–R interval 0·4 sec., soon after carotid sinus pressure had been stopped.

auricular and ventricular rhythms maintained as before. After all this pressure on the neck had stopped, the patient was in a distressed condition, but normal rhythm had returned with a P–R interval of 0·4 sec. (lower tracing, Fig. 6). Treatment of this patient with eumydrine, ephedrine, and digitalis in turn had no certain effect on the frequency of the Stokes-Adams attacks.

Case 3. A man, aged 69, subject to attacks of loss of consciousness since 1938, was said to have had rheumatic fever when 7 years old; there was no evidence of rheumatic heart disease, but some hypertension with left ventricular hypertrophy was present. When first seen in 1945, he had normal rhythm and it was not until 1948 that a record showing complete block was obtained. About this time, during the taking of a routine tracing which showed normal rhythm, a ventricular extrasystole occurred and this was immediately followed by ventricular standstill, loss of consciousness, and a convulsion (Fig. 7). Immediately after the attack, the tracing was resumed and showed normal sinus rhythm and the A-V conduction within normal limits. The patient himself preferred his pulse slow (complete block) rather than quick (normal rhythm) as then he found he had fewer attacks and he had noticed that if he raised his left arm, he would lose con-

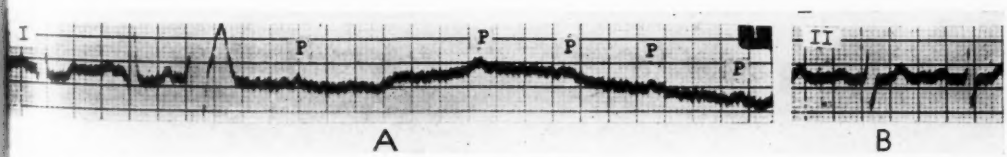

FIG. 7.—Case 3. Man, aged 69. Normal rhythm, normal P–R interval. (A) Ventricular standstill follows a ventricular extrasystole (lead I), causing a Stokes-Adams attack. (B) Normal rhythm and conduction are resumed immediately after the attack.

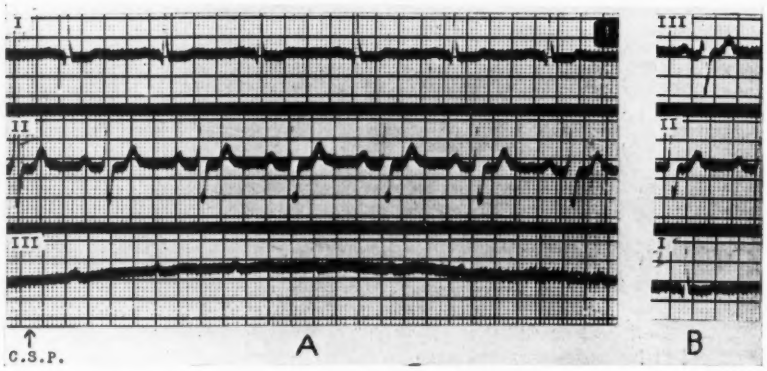

FIG. 8.—Case 3. (A) Ventricular standstill produced immediately by carotid sinus pressure. (B) Normal rhythm and conduction recorded as soon as the attack was over.

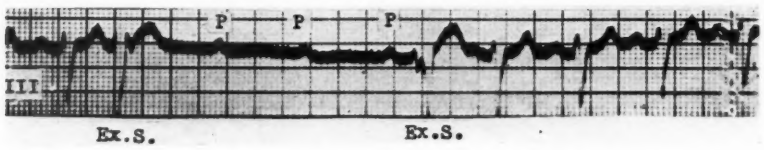

FIG. 9.—Case 3. Ventricular standstill for three cycles following an extrasystole; the first beat after the standstill is also aberrant.

sciousness but not if he raised his right arm. Carotid sinus pressure was tried first on the right without effect, and then on the left with immediate ventricular standstill (Fig. 8). The almost instantaneous effect of the pressure is shown in the record, pressure on the carotid sinus coinciding with depression of the lever to start the recording drum. The beginning of limb movements is shown by the unsteadiness of the tracing after about 5 seconds. During this time the auricular rate increased from 75 to 100 a minute. The tracing was resumed as soon as possible after the attack and was exactly the same as before it, with sinus rhythm, rate about 75 and normal A-V conduction time. For some months all records showed normal rhythm; then one was obtained showing ventricular standstill for three cycles after a ventricular premature beat, the resumption of normal rhythm being preceded by another ventricular premature contraction (Fig. 9).

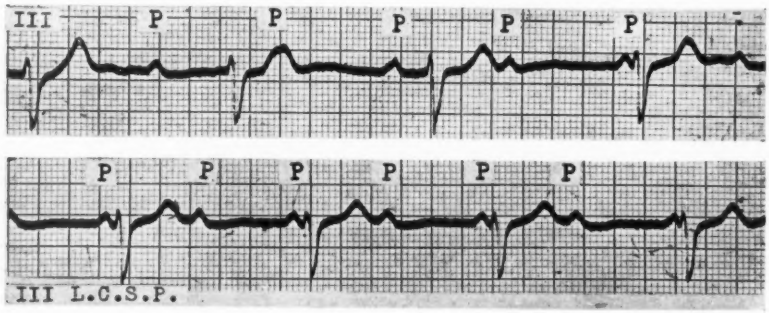

FIG. 10.—Case 3. Upper tracing: complete heart block. Lower tracing: left carotid sinus pressure causes no auricular or ventricular slowing.

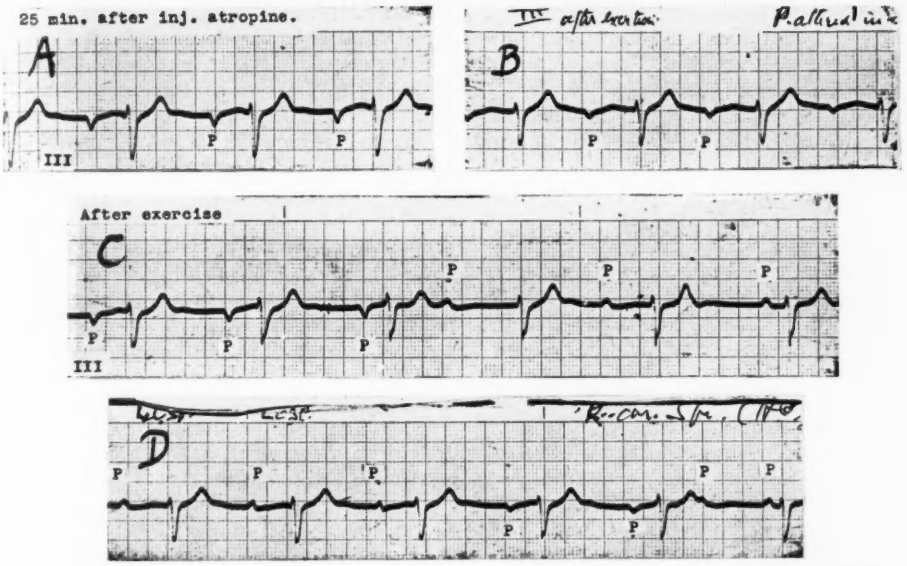

FIG. 11.—Case 3. (A) After injection of atropine gr. 1/100, complete heart block with auricular and ventricular rates almost the same; P inverted. (B) After exertion P altered in shape. (C) After more exertion P at first negative becomes upright; 2 : 1 sino-auricular block; complete A-V block. (D) Complete block and 2 : 1 sino-auricular block; carotid sinus pressure causes temporary inversion of P; sino-auricular block disappears at end of tracing.

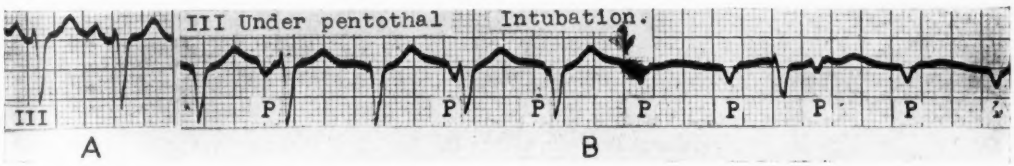

FIG. 12. Case 3. (A) Normal rhythm and normal conduction, rate 105 a minute. (B) Under pentothal anæsthesia, ventricular rate unchanged, P negative; probably nodal rhythm: passing of tracheal tube (shown by arrow) produced complete block.

The following day, auricular fibrillation was recorded at which time neither arm raising nor carotid sinus pressure had any effect. When complete block was present, carotid sinus pressure whether left or right was incapable of causing ventricular standstill, nor did it slow the auricle (Fig. 10). Two to one sino-auricular block occurred from time to time; it would appear after exertion and after an injection of atropine (Fig. 11); at other times the P wave became inverted or biphasic. While waiting to be given an anæsthetic, this patient had sinus tachycardia with normal A-V conduction (Fig. 12, A). After pentothal P became inverted, the ventricular rate being much the same. At the moment a McGill's tube was passed through the nose into the trachea, there was a transition to complete A-V dissociation (Fig. 12, B).

DISCUSSION

The commonest causes of the Stokes-Adams attack are believed to be: (1) transition from normal rhythm to high-grade block; (2) slowing of the idio-ventricular rhythm in the course of complete block; and (3) abnormal ventricular rhythms such as ventricular tachycardia and fibril-

lation followed by standstill. Of the three cases of ventricular standstill described here occurring as an episode in the course of normal rhythm, two showed varying degrees of heart block from time to time. They had also extreme sensitivity of the carotid sinus at times, but this was only found when normal rhythm was present. Then quite slight pressure on the carotid sinus—one side was more responsive than the other—was capable of arresting the ventricle within about a second, followed immediately by loss of consciousness and then within 5 to 8 seconds by tonic contraction of the limbs. The term loss of consciousness is not a precise one, but it is certain that immediately after the ventricle stopped beating, the patients began to lose consciousness, while the onset of tonic limb contractions can be measured accurately from the movement of the baseline of the tracing. The immediate impairment of consciousness may not be entirely due to the fall in cerebral blood flow, and it is possible that a direct stimulation of the cerebral circulation plays a part as suggested by Weiss and Baker (1933) to explain cases in which carotid sinus stimulation caused syncope without slowing of the heart rate or fall in blood pressure. The extreme sensitivity of the conducting tissues to nerve impulses is shown by the induction of mild attacks by merely raising the arm, or changing posture. These events occurred only when normal rhythm was present and even then the response to carotid sinus pressure varied much from day to day and even from hour to hour. However, the position was very different when complete block was present; then carotid sinus stimulation was without effect on the ventricle and usually on the auricle also, though it might slow its rate a little or displace the site of impulse formation. It appears that when normal rhythm is present, the reflex from the carotid sinus acts on the upper part of the bundle of His and is temporarily incapacitated, although immediately before and after it conducts perfectly. On the other hand, when complete block is present, the centre governing the ventricle, situated lower in the bundle, is immune from the effects of the reflex. An interesting observation is the onset of ventricular standstill after a ventricular extrasystole. Might this result from fatigue of the bundle by the premature retrograde stimulation, or alternatively might a nervous impulse simultaneously act upon the ventricle and the bundle to produce both effects?

The diagnosis of epilepsy from loss of consciousness due to paroxysmal ventricular standstill may be difficult from the history alone, even if a description of the attacks by a good eye-witness is available. A short standstill simulates petit mal very closely, but a longer one leading to complete loss of consciousness and convulsion will usually differ from grand mal in the facial pallor rather than congestion, in the facial flush as the attack ends, and in the more rapid return of full consciousness. The elderly subject with a history of loss of consciousness, even over many years, and even though his cardiogram at first shows not the least sign of block, may yet be suffering from paroxysmal ventricular standstill or other kind of heart block. For such a patient, carotid sinus pressure might settle the diagnosis, though this is hardly a method to be used indiscriminately. Apart from this, the true diagnosis will probably be revealed by continued observation, as sooner or later ordinary forms of auriculo-ventricular block will make their appearance.

It used to be thought that the heart block of chronic heart disease was usually permanent, but it is now clear that in many the rhythm passes back and forth from block to normal over long periods of years, the duration of each varying from seconds to months. In addition to the basic structural lesion, therefore, other factors must be involved and among these are reflexes from the carotid sinus, pharynx, and œsophagus, and perhaps impulses arising in the brain itself as a result of emotional disturbance.

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THE EXERCISE TEST IN PATENT DUCTUS ARTERIOSUS

BY

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The clinical diagnosis of patent ductus arteriosus rests primarily upon the presence of the characteristic continuous murmur first described by Gibson (1906), but information gained by a study of the blood pressure may strengthen the diagnosis in some cases.

Gordon (1926) appears to have been the first to draw attention to abnormalities of blood pressure in patent ductus arteriosus. He predicted that low arterial tension, which was a prominent finding in his patient, would prove to be a common observation. Although this early impression has been confirmed by numerous observers, the interpretation of much of the information relating to blood-pressure studies in patent ductus remains uncertain because of the lack of controlled observations. This uncertainty in interpretation applies particularly to the changes in diastolic blood pressure after exercise. Following the introduction of the exercise test by Bohn (1938), a fall in diastolic pressure after effort has been widely sought as an ancillary sign of patent ductus arteriosus—particularly in recent years since the value of this test has been emphasized by Lewicki (1940), Gilchrist (1945, 1946), and others.

The purpose of this communication is to present the results of controlled observation on the effect of exercise upon the blood pressure in patent ductus arteriosus before and after surgical closure of the ductus, and to define more clearly the limitations and value of the exercise test in the diagnosis of this condition.

Clinical Material and Methods

Twenty-six consecutive patients with uncomplicated patency of the ductus arteriosus were studied before operation and at the end of the second week after successful ligation. All but three of the patients were girls or women and the average age was 13 years (6 to 26 years). The diagnosis, confirmed at operation, was made on the basis of a Gibson murmur, absence of cyanosis and clubbing, a palpable femoral pulse, and an electrocardiogram that was either physiological or showed only left ventricular preponderance.

Three groups of controls were studied: 26 healthy subjects of an age and sex corresponding to that of the patients, 100 healthy subjects of widely differing ages, and 24 patients recovering from various major surgical operations other than for closure of a patent ductus arteriosus or an arteriovenous fistula elsewhere.

Measurement of Blood Pressure. The right brachial blood pressure was recorded by the cuff method using a standard mercury sphygmomanometer. The joint recommendations of the British Cardiac Society and the American Heart Association (1939) for the standardization of blood pressure measurement were adopted, and the British Committee's recommendation for recording diastolic blood pressure was followed. Blood pressure readings were invariably taken with the subject recumbent and by the same observer.

Resting blood pressure records were obtained in the following manner: subjects lay comfortably on a couch in a quiet room; the cuff was applied to the right arm and a blood pressure record was taken. A period of rest of at least 20 minutes was allowed, and blood pressure records were then taken at three-minute intervals until systolic and diastolic levels remained constant. These figures were accepted as the resting blood pressure.

A standard exercise test, calculated to induce tachycardia and mild or moderate distress as recommended by Gilchrist (1945), was employed. With the sphygmomanometer cuff in position, the subject stepped briskly 24 times on to a stool 15 to 18 inches high, alternating the stepping foot after each six ascents. Immediately after the exercise the subject lay on the couch; the blood pressure was taken within 30 seconds of the end of the exercise and at minute intervals for five minutes.

Since changes in the blood pressure, and particularly the diastolic pressure, are most evident immediately after exercise, this study is concerned with the readings taken within 30 seconds.

Observations before Operation

The mean resting systolic pressure in patent ductus is greater than in controls (Table I), and the difference between the means is regarded as significant. As might be expected in ductus cases, resting diastolic readings are significantly lower and pulse pressures significantly higher than in controls.

TABLE I

Mean Blood Pressure at Rest and After Exercise

Blood pressure	Patients with Patent Ductus Arteriosus (mm. Hg)	Controls (mm. Hg)	*t*	*P*
Systolic				
Rest	114±11	107±5	3·12	<0·01
Exercise	149±23	143±17	1·68	>0·05
Diastolic				
Rest	57±11	68±6	4·63	<0·001
Exercise	58±14	67±17	2·57	<0·02
Pulse				
Rest	57±16	39±7	5·84	<0·001
Exercise	91±28	76±17	2·93	<0·01

± Followed by a number represents the standard deviation of the observations.

After exercise, the mean systolic readings are set at a higher level, but the difference between the means is not significant in contrast with the resting figures. The difference between the mean diastolic pressures is less than at rest. The mean pulse pressure is significantly higher in the cases than in the controls, but the difference is less obvious than that of the resting figures. There is no indication that exercise lowers the mean resting diastolic pressure in patent ductus; in fact, the figures suggest a rise rather than a fall.

A fall in diastolic pressure after exercise was twice as frequent in healthy subjects as in patients with patent ductus; the incidence of a stationary diastolic pressure was comparable in the two groups, but a rise in diastolic pressure was twice as common among patients as compared with controls (Table II). Of six cases of patent ductus showing a fall in diastolic pressure, in only two did this exceed the maximum fall noted in controls, namely, 10 mm. Hg, and in these two cases it was profound (Fig. 1).

In order to study further the behaviour of the diastolic pressure following exercise in health, 100 normal subjects of widely differing ages were examined (Table II). Of the 37 subjects who showed a fall in diastolic pressure, the majority gave values of 5 or 10 mm. In three instances,

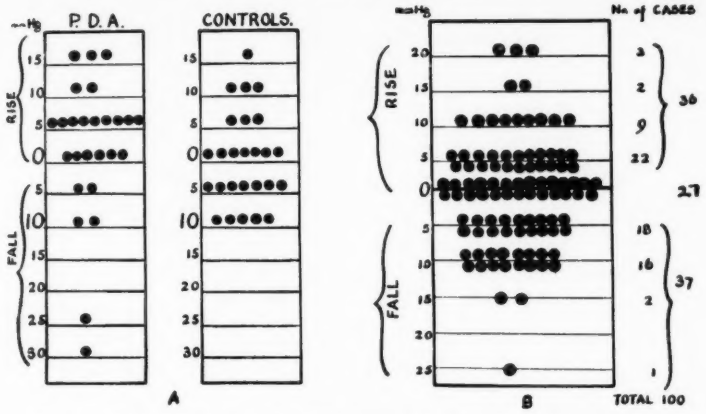

FIG. 1.—Change in diastolic blood pressure after exercise. (A) In 26 cases of P.D.A. and 26 controls. (B) In 100 healthy subjects.

however, the fall in diastolic pressure exceeded 10 mm.; and in one of these it was profound (Fig. 1). In each of these three the exercise test was repeated and the same respective fall was recorded. When the change in diastolic pressure after exercise in cases of patent ductus (Fig. 1) is compared with that in 100 normal subjects, a fall in the diastolic pressure exceeding 10 mm. might appear to be relatively more common in cases of patent ductus. Statistically, however, there is no real difference between the behaviour of the two groups ($t=1{\cdot}48$).

In this preoperative investigation, the exercise test offered little information of value in diagnosis, over and above that which was apparent from a study of the resting blood pressure readings in cases of patent ductus arteriosus, and statistical evidence that the test is of any real value is lacking.

OBSERVATIONS AFTER OPERATION

Touroff and Vessell (1940) state that a Bohn exercise test was carried out 26 days after surgical division of an infected ductus arteriosus in a patient with a continuous murmur that persisted after the operation. Failure of the diastolic pressure to fall after exercise by more than 2 mm. Hg indicated, in the authors' opinion, absence of an arterio-venous shunt. This report prompted an enquiry into the effect of exercise upon the diastolic pressure in the present series during convalescence from operation. It was possible to study 15 of the 26 cases in this way two weeks after surgical ligation of the ductus when the patients had been ambulant for at least a week. In no case were there murmurs suggesting recanalization of the ductus and subsequent follow-up has shown the operation to have been successful in every case. A standard exercise test, performed two weeks after the operation, caused the diastolic pressure to fall in 7 of the 15 cases studied, despite lack of supporting evidence of ductal recanalization (Table II).

In order to allow for any influence that the trauma of operation and post-operative immobilization might have had upon the blood pressure in the cases studied, a control group of 24 patients were examined at the end of the second week of convalescence from various major surgical operations. The resting blood pressure and the effect of exercise upon it were determined by methods already described. Among surgical controls a fall in diastolic pressure was unusual and in three-quarters of them the diastolic pressure was raised by exercise. Of the seven ductus cases in which the diastolic pressure was lowered by exercise, the fall exceeded 10 mm. in four (Fig. 2); in the other three a fall of 10 mm. or less lay within the range observed in surgical control cases and in 97 per cent of normal subjects (Fig. 1).

TABLE II

INFLUENCE OF EXERCISE UPON THE RESTING DIASTOLIC PRESSURE

Age group (years) Healthy subjects	No. of cases	Change in diastolic B.P.		
		Fall	Rise	No change
5–10	17	2	10	5
11–20	41	14	17	10
21–30	12	7	2	3
31–40	10	5	3	2
41–50	7	4	1	2
Over 50	13	5	3	5
Totals	100	37	36	27
26 cases of P.D.A. (before operation		6	14	6
26 controls		12	7	7
15 cases of P.D.A. (after operation)		7	4	4
24 surgical controls		3	18	3

The difference between the means of the change in diastolic pressure after exercise in ductus cases after operation and in surgical controls is clearly significant. Furthermore, a fall in diastolic pressure exceeding 10 mm. occurred more frequently *after* ductal ligation in these 15 cases than it did in the 26 cases *before* operation when the ductus was patent. The difference in the behaviour of these two groups is regarded as real and unlikely to have been due to chance (Fig. 2). The remarkable fall in diastolic pressure after exercise that followed successful closure of the ductus appeared to be a phenomenon associated with the early post-operative period; for in eight patients in whom the exercise test was repeated many months after the operation, this tendency for the diastolic pressure to fall steeply in early convalescence had either disappeared completely, or else the fall was within the range common to health (Fig. 3).

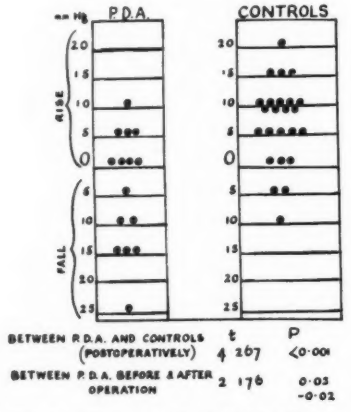

FIG. 2.—Change in diastolic blood pressure after exercise in 15 cases of ductus arteriosus and in 24 controls, two weeks after operation.

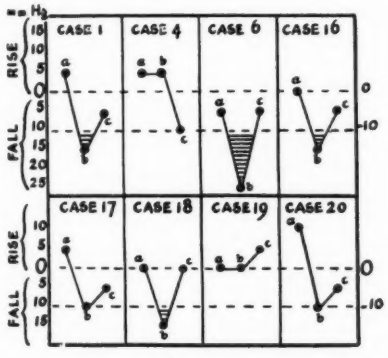

FIG. 3.—The change in resting diastolic blood pressure following exercise in 8 cases of patent ductus—(a) before operation, (b) two weeks after ligation of the ductus, (c) two months or more after operation.

Characteristic changes in the blood pressure, before, during, and after the operation, with special reference to the effect of exercise upon the diastolic pressure before ligation and during convalescence, are shown in Fig. 4. In the case illustrated, the preoperative fall in diastolic pressure after exercise lay within the range observed in health; in early convalescence the fall was profound (25 mm.), and in late convalescence it was minimal. Although the fall in diastolic pressure in early convalescence was great, the diastolic reading immediately after exercise did not fall below the *resting* diastolic pressure before operation: exercise, in fact, appeared to have momentarily abolished the steep but temporary rise in diastolic pressure that invariably followed closure of the ductus in all our 26 patients. The other cases that showed a marked fall in diastolic pressure after exercise in early convalescence behaved in the same way.

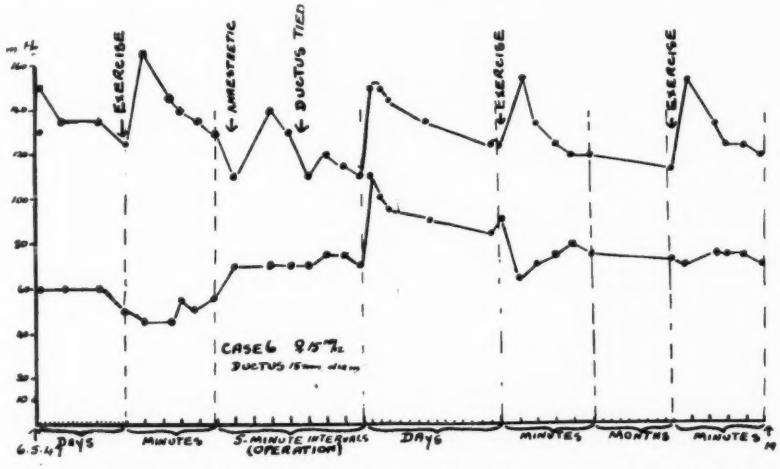

FIG. 4.—Composite graph showing changes in blood pressure before, during, and after operation in patent ductus arteriosus.

SUMMARY AND CONCLUSIONS

Controlled observations of the effect of a standard exercise upon the resting blood pressure were made in 26 consecutive cases of uncomplicated patent ductus arteriosus before and after surgical ligation. The mean resting systolic pressure was significantly higher, and the mean diastolic pressure significantly lower in patients with patent ductus arteriosus than in control subjects of corresponding age and sex.

Exercise caused no significant change in the mean diastolic pressure either of ductus cases or controls. A fall in diastolic pressure after exercise was twice as common among controls as in cases of patent ductus. In only two cases of patent ductus did the fall in diastolic pressure exceed 10 mm. Hg. In a group of 100 healthy subjects a fall in diastolic pressure after exercise was recorded in 37 per cent; frequently the pressure fell by 10 mm., and occasionally the fall was profound.

The exercise test, as judged by a fall in the resting diastolic pressure, was suspected of being positive in only 2 out of the 26 cases of patent ductus, that is, in one-third of those in which a fall in diastolic pressure was recorded. Since a fall in diastolic pressure after exercise is common in health, although rarely greater than 10 mm., it is suggested that an exercise test, carried out in proved or suspected cases of patent ductus arteriosus, should be regarded as giving a positive response only when the diastolic pressure falls by 15 mm. or more.

In this investigation the exercise test offered little information of value in diagnosis, over and above that which was apparent from study of the resting blood-pressure readings of patients with patent ductus arteriosus, and statistical evidence that the test is of any real value is lacking.

Two weeks after successful ligation of the ductus arteriosus a fall in the diastolic pressure after exercise was observed in almost half the cases. This unexpected finding, which appeared to be transitory and was found only in the early period after operation, differed significantly from the changes observed in a control group of cases in which the diastolic pressure was raised or remained stationary in 90 per cent. A fall in the diastolic pressure after exercise was significantly commoner and more profound when the ductus was closed, than it was before operation.

No satisfactory explanation for the behaviour of the diastolic pressure after exercise during convalescence from operation is apparent, but the phenomena observed permit the following inference, namely: that a sharp fall in the diastolic pressure after exercise, which follows closely on the operation, is no criterion that the ductus has recanalized.

I am indebted to Dr. William Evans and Professor John McMichael for criticism of this paper; to Dr. D. A. Mitchison for statistical help and advice, and to Mr. C. Vernon Thompson and Mr. W. P. Cleland for allowing me to examine patients under their care. To the patients and others, whose co-operation made this study possible, and to Miss Helen Wilson and Mr. R. J. Marshall, who prepared the diagrams, I extend my thanks.

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CIRCULATORY CHANGES IN MITRAL STENOSIS AT REST AND ON EXERCISE

BY

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There is some increase in the pulmonary artery pressure in many patients with mitral stenosis and this pressure may rise considerably on exercise as was first shown by Hickam and Cargill (1948). Gorlin and Gorlin (1951) have described a method of calculating the area of the mitral orifice in life and Gorlin *et al.* (1951 *a* and *b*) have attempted to evaluate the factors causing this pulmonary hypertension at rest and on exercise. Although in these cases, the stenosed mitral valve must be the primary cause, other changes that may occur in the pulmonary vasculature or in the pulmonary blood volume may also be of importance. Lagerlöf *et al.* (1949) and Borden *et al.* (1949) using the Hamilton method, injecting dye directly into the pulmonary artery, showed no increase in the pulmonary blood volume in patients with mitral stenosis at rest. Kopelman and Lee (1951) verified these findings with dye injected into an antecubital vein and also showed no significant increase in the intrathoracic blood volume in mitral stenosis even when in congestive cardiac failure. This was in contrast with patients in left ventricular failure who showed a well marked increase in intrathoracic blood volume.

The Hamilton dye method has been used in a further study of patients with mitral stenosis to determine the changes in cardiac output and intrathoracic blood volume that occur during mild exercise.

Material and Methods

Sixteen patients with mitral stenosis were investigated. Some of these had auscultatory signs of aortic valve involvement but mitral stenosis was considered to be the predominant lesion. None had clinical signs of congestive cardiac failure at the time of the investigation. Previous experience has shown that the presence of a giant left atrium or of tricuspid regurgitation prevents a reliable result with the method used, and no patient investigated had either of these conditions. Nine subjects without evidence of cardiovascular disease were similarly investigated.

The Hamilton dye method consists of the injection of a known amount of dye (Evans Blue T 1824) into an antecubital vein and the collection of rapidly timed arterial samples. From these a time-concentration curve can be constructed and the cardiac output and mean circulation time calculated as described by Hamilton *et al.* (1932). By the application of Stewart's formula (1921) the volume of blood between injection and sampling points can be determined and this has been referred to as the " intrathoracic blood volume."

In a series of five duplicate tests at rest, the coefficient of variation for the intrathoracic blood volume was found to be 6·5 per cent: although the number is small, changes in the intrathoracic blood volume of more than 13 per cent are probably significant. Similarly changes in the cardiac output of the same order are probably significant, the summation of errors in the technique being 6 per cent (Hamilton *et al.*, 1948; Kopelman and Lee, 1951). It has been found that the cardiac output obtained by this method corresponds

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closely with that obtained by the direct Fick principle (Hamilton *et al.*, 1948; Lagerlöf *et al.*, 1949; Kopelman and Lee, 1951).

Patients were investigated in their beds, comfortably seated at an angle of 30 to 40 degrees. They were fasted but not sedated and the procedure was made painless by careful local infiltration over both puncture sites. The test was done first at rest, as described by Kopelman and Lee (1951), and then repeated fifteen minutes later during leg exercises. These were performed by alternately compressing and releasing two foot pumps arranged on a support which could be fitted to the end of the bed. The duration of exercise was approximately five minutes, but was less in the more severe cases of mitral stenosis as it was discontinued as soon as there was much dyspnœa. No real attempt was made to standardize the exercise because of this variation in functional capacity. The indwelling arterial needle was left *in situ* for both tests and it was found that with a closely fitting stilette, which extended 1 or 2 mm. beyond the needle tip, adequate samples could be obtained for the second study in most cases.

All patients had teleradiograms taken at rest and immediately after exercise. From these the cardiothoracic (C/T) ratio was determined by the method described by Meneely and Chesnut (1947). The pulmonary artery was noted as being normal, enlarged, or very enlarged, but no measurement was attempted. In some of these patients cardiac catheterization was performed and intracardiac pressure recorded, but these were not performed on the same day as the dye test.

Results in Normal Controls

The results in patients with normal cardiovascular systems are shown in Table I. The mean resting cardiac index was 3·3 litres which increased on exercise to 4·3 litres per square metre of body surface. Most cases showed a significant increase in the cardiac index on exercise, but this was variable in extent, probably because of differences in training and fitness, as has been found by Riley *et al.* (1948) and Dexter *et al.* (1951) using the catheter technique.

The intrathoracic blood volume index at rest was 1·22 litres and increased on exercise to 1·43 litres per square metre of body surface. Four of the nine subjects, however, showed no significant rise in intrathoracic blood volume, although in three of these (C43, C27, and C37) there was a marked rise in cardiac output. The mean circulation time in these patients decreased more than in the others. This suggests that in mild exercise in normal subjects, the increase in blood flow can cause either an increase in the intrathoracic blood volume or a speeding up of the circulation in the thorax or both.

Results in Mitral Stenosis

Table II shows the results obtained in patients with mitral stenosis arranged in descending order of their cardiac indices. Stead *et al.* (1945) found that the average cardiac index at rest in a group of normal subjects was 3·3 with a range of 2·3 to 4·1 litres per square metre of body surface. In the present series the lower limit for the normal resting cardiac index has been taken as 2·5 litres and the patients with mitral stenosis subdivided into two groups: (*a*) those with a normal cardiac index at rest, that is greater than 2·5 litres, and (*b*) those with a low resting cardiac index, that is less than 2·5 litres per square metre.

(*a*) *Normal Resting Cardiac Index.* Nine patients were found to be in this group with a mean cardiac index of 3·4 litres. Four of these were able to increase their cardiac index on mild exercise to more than 4·3 litres, i.e. a slightly greater cardiac output response than the average normal. All four showed some increase in intrathoracic blood volume, with the mean circulation time remaining the same or decreasing slightly. In the other five patients in this group who had a slightly lower cardiac index at rest, the increase in cardiac index on exercise was less and in no case did it reach 4·0 litres per square metre; in two there was no significant rise. All but one of these showed a prolongation of the mean circulation time on exercise with a corresponding increase in the intrathoracic blood volume. This prolongation in mean circulation time was not found so consistently in any other group.

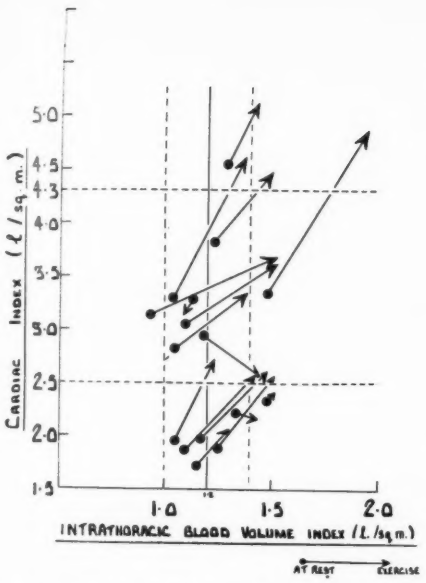

FIG. 1.—Changes in the cardiac index and intrathoracic blood volume index in exercise in mitral stenosis. The mean value for the intrathoracic volume index in 9 normal subjects is shown at 1·2 litres with the vertical broken lines indicating the standard deviation of these observations.

been arranged in the same order as before. It is apparent that the cases with low cardiac outputs at rest have the larger hearts as indicated by the increase in the cardio-thoracic ratio. This inverse relationship between cardiac output and heart size in mitral stenosis is well shown in Fig. 3 which is obtained from the present data and those of Kopelman and Lee (1951). This relationship does not hold for patients with left ventricular failure ($r=-0{\cdot}16$; $p>0{\cdot}1$). On exercise no measurable increase in the cardio-thoracic ratio in any patient occurred although in a few cases the main pulmonary artery appeared a little more prominent.

A previous history of congestive cardiac failure was present in all patients showing low resting cardiac outputs. Some with normal cardiac outputs also gave histories of mild congestive failure but only those with poor exercise responses. In these patients auricular fibrillation was nearly always present.

Patients have also been classified into the grades of functional capacity defined by the New York Heart Association (1939). Many, however, had functional capacities that varied from time to time under varying circumstances and it was found convenient to indicate this by placing them between the two relevant grades. It can be seen that the functional capacity appeared to decrease as the resting cardiac index fell.

(*b*) *Low Resting Cardiac Index.* There were seven patients in this group with a mean cardiac index at rest of 2·0 litres, although five actually had cardiac indices less than this. All except two of these patients showed some rise in the cardiac index on exercise, the mean being 2·4 litres: none were able to reach 3·0 litres per square metre. The intrathoracic blood volume rose in all cases on exercise except in the two showing no change in cardiac output. This was accompanied by a small decrease in the mean circulation time. The mean increase was less than in the previous group but the difference was not statistically significant ($t=1{\cdot}56$; $p>0{\cdot}1$).

The changes in cardiac output and intrathoracic blood volume that occur on exercise are diagrammatically shown in Fig. 1. From the results in the present series and from those of Kopelman and Lee (1951) there appears to be a close relationship between the resting cardiac output and the mean circulation time in normals and in mitral stenosis whether in congestive failure or not. This is demonstrated in Fig. 2. Thus the mean circulation time is within the normal range in the patients with mitral stenosis with normal resting cardiac indices but becomes greatly prolonged in those with low resting values.

CLINICAL FEATURES

In Table III some of the clinical and radiological data have been listed; the patients having

DISCUSSION

Wide differences in cardiac output and mean circulation time were present in the normal group and in those patients with mitral stenosis who still had normal resting cardiac outputs (Tables I and II). This could be explained by mild apprehension felt by some patients during the test so

TABLE I

NORMALS

No.	Pulse		Output			Mean Circulation Time			Intrathoracic Blood Volume				
			Rest	Exercise	Change				Rest		Exercise		
	Rest	Exercise	C.I. l./m.²	C.I. l./m.²	C.I. l./m.²	Rest sec.	Exercise sec.	Change sec.	l.	Index l./m.²	l.	Index l./m.²	Change Index l./m.²
C43	60	76	2·53	3·94	+1·61	27	20	−7	2·36	1·24	2·48	1·31	+0·07
C13	76	104	2·8	5·9	+3·10	22	21	−1	1·51	1·02	3·01	2·02	+1·0
C24	84	104	2·98	3·30	+0·32	29	26	−3	2·48	1·42	2·39	1·37	−0·05
C32	72	96	3·26	4·20	+1·94	26	24	−2	2·6	1·44	3·0	1·66	+0·22
C27	84	102	3·35	4·75	+1·40	21	14	−7	1·93	1·15	1·85	1·10	−0·05
C36	64	68	3·44	4·00	+0·56	17	18	+1	1·76	0·98	2·16	1·21	+0·23
C42	60	72	3·53	3·66	+0·13	21	22	+1	1·98	1·21	2·19	1·33	+0·12
C37	76	86	3·56	4·57	+1·01	20	16	−4	2·06	1·16	2·16	1·22	+0·06
C14	76	100	4·25	4·61	+0·36	20	21	+1	2·61	1·40	3·05	1·64	+0·24
Mean Values			3·30	4·33	+1·03	22·5	20·2	−2·3	2·1	1·22	2·47	1·43	+0·22
Standard Deviation of Observations			±0·50	±0·73		±4·2	±3·9			±0·20		±0·29	±0·96

C.I.=Cardiac index (litres/min. per square metre of body surface).

TABLE II

MITRAL STENOSIS

No.	Pulse		Output			Mean Circulation Time			Intrathoracic Blood Volume					R.V.P. or P.A.P.	
			Rest	Exercise	Change				Rest		Exercise		Change		
	Rest	Exercise	C.I. l./m.²	C.I. l./m.²	C.I. l./m.²	Rest sec.	Exercise sec.	Change sec.	l.	Index l./m.²	l.	Index l./m.²	Index l./m.²	Rest mm.	Exercise mm. Hg
C35	78	108	4·55	5·1	+0·55	17	16·0	−1	2·34	1·29	2·42	1·42	+0·14		
C33	90	124	3·83	4·46	+0·63	20	20	0	2·06	1·23	2·49	1·49	+0·26		
C16	52	96	3·73	4·86	+1·13	24	23	−1	2·6	1·48	3·4	1·94	+0·46		
C12	72	104	3·30	4·60	+1·3	19	17	−2	1·72	1·04	2·26	1·37	+0·33	36/0	57/?
C34	104	104	3·27	3·14	−0·13	21	21	0	1·52	1·12	1·46	1·08	−0·04		
C17	104	124	3·14	3·68	+0·54	18	25	+7	1·47	0·93	2·4	1·52	+0·59		
C29	84	80	3·04	3·61	+0·57	21	25	+4	1·77	1·09	2·47	1·52	+0·43		
C41	112	120	2·94	2·57	−0·37	25	34	+9	1·77	1·19	2·13	1·44	+0·25		
C10	90	126	2·82	3·33	+0·51	22	25	+3	1·67	1·05	2·2	1·38	+0·33	66/1	74/4
Mean Values			3·4	3·93	+0·53	21	23	+2	1·88	1·16	2·36	1·46	+0·30		
Standard Deviation			±0·56	±0·85		±3	±5			±0·17		±0·24	±0·18		
C8	—	—	2·36	2·36	0	38	38	0	2·4	1·49	2·4	1·49	0	104/6	130/12
C40	72	92	2·22	2·15	−0·07	36	40	+4	1·87	1·34	2·0	1·43	+0·09		
C30	78	115	1·99	2·68	+0·69	35	33	−2	1·82	1·16	2·3	1·47	+0·31	78/14	—
C38	76	124	1·97	2·70	+0·73	32	29	−3	1·60	1·05	1·85	1·22	+0·17	54/?	90/?
C23	66	112	1·90	2·56	+0·66	39	35	−4	1·90	1·25	2·30	1·51	+0·26	45/3	63/5
C4	—	—	1·87	2·58	+0·71	35	33	−2	1·7	1·10	2·2	1·42	+0·32	155/14	163/35
C31	54	90	1·73	2·06	+0·33	40	38	−2	1·9	1·15	2·15	1·30	+0·15		
Mean Values			2·01	2·44	+0·44	36	35	−1	1·88	1·22	2·17	1·41	+0·19		
Standard Deviation			±0·22	±0·27		±3	±4			±0·15		±0·10	±0·11		

R.V.P. = Right ventricular pressure.
P.A.P. = Pulmonary artery pressure.

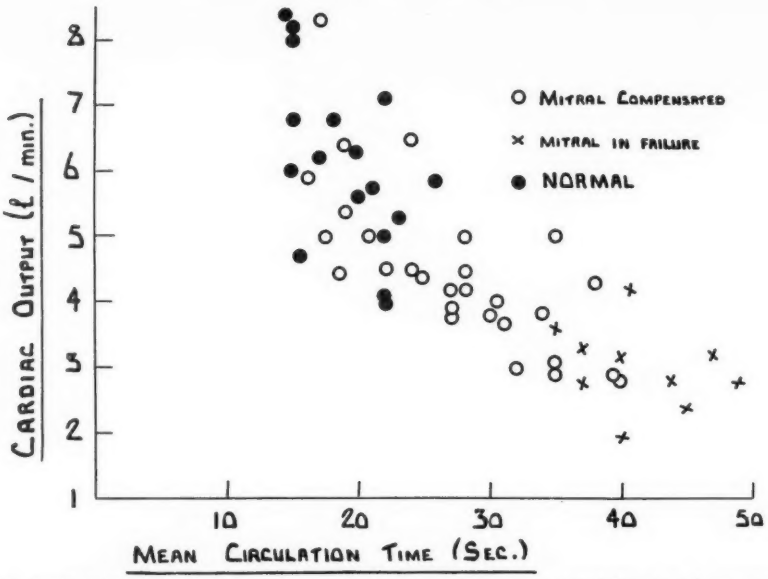

FIG. 2.—Relation between the resting cardiac output and the mean circulation time in normals and in mitral stenosis. From present data and that of Kopelman and Lee (1951).

that they were not strictly basal. Patients with poorer exercise tolerance who had the lower cardiac outputs showed less variation at rest and on exercise as their range of cardiac output was more restricted.

The Intrathoracic Blood Volume. In a previous series (Kopelman and Lee, 1951), no statistically significant difference was found in the intrathoracic blood volume of patients with mitral stenosis and that of normal subjects. The present series confirms this.

The boundaries of the volume of blood referred to as the intrathoracic blood volume cannot be precisely defined, but have been discussed by Hamilton *et al.* (1932). It consists of the *circulating* blood in four main compartments, the great veins, the heart, the pulmonary vessels, and the aorta and arteries to the collection point. Cardiac enlargement, as demonstrated by an increase in cardiothoracic ratio was present in 12 of the 16 cases with mitral stenosis and it is therefore probable that these hearts contained more blood than normal. The systemic arterial component is unlikely to have been greatly reduced, especially as many of the patients had normal cardiac outputs. Since in the mitral stenosis patients the intrathoracic blood volume was not greater than normal and the hearts generally contained more blood, there must have been a reduction in the blood volume either in the pulmonary vessels or in the great veins. None of these patients had clinical evidence of congestive failure at the time of the test which might increase the venous component, and it seems unlikely that this volume was less than normal. Thus using this indirect method of deducing the pulmonary blood volume, we reach the rather surprising conclusion that in mitral stenosis at rest the *circulating* blood volume in the pulmonary vessels is actually reduced. Most of these patients, however, on radioscopy had some enlargement of the main pulmonary arteries, so that if a reduction in pulmonary blood volume does occur, it follows that it must be in the small vessels.

The Effects of Exercise. In the small group of normal subjects studied the cardiac output rose in most cases on exercise. The intrathoracic blood volume increased in some, but in others did not significantly change; in these latter the mean circulation time fell. It has been shown that

TABLE III

CLINICAL FEATURES

No.	Sex	Age	Surface Area sq. m.	Diagnosis	Rhythm	B.P.	Function Classification I to IV	Duration of Symptoms	Patients who have been in Failure	Radiology	
										C/t Ratio	Pulmonary Artery
C35	M.	26	1·82	M.S., A.I.	R.	110/60	I	—	No	0·46	0
C33	M.	40	1·67	M.S., Emphysema	R.	130/70	II	Brorchitis 30 yrs.	No	0·56	++
C16	M.	34	1·75	M.S., A.S.	R.	90/60	II	9 yrs.	No	0·45	±
C12	F.	23	1·65	M.S.	R.	120/75	II	2 yrs.	? slight 1950	0·47	+
C34	F.	43	1·36	M.S.	A.F.	145/85	III	1 until 3/12 ago	Slight 1951	0·57	0
C17	F.	40	1·58	M.S., A.I.	R.	115/75	II→III	4 yrs.	Slight œdema O.A.	0·40	+
C29	F.	60	1·62	M.S., A.I.	A.F.	120/?	II→III	10 yrs.	Early failure O.A.	0·57	+
C41	F.	34	1·48	M.S., M.I.	A.F.	105/70	II→III	8 yrs.	J.V.P. slightly+O.A.	0·61	0
C10	F.	45	1·59	M.S., A.I.	A.F.	154/106	II→III	4 yrs.	Slight œdema O.A.	0·58	+
C8	M.	36	1·61	M.S.	R.	120/80	III	3 yrs.	Œdema since 1948	0·58	+
C40	F.	51	1·39	M.S., A.I.	A.F.	140/100	III→IV	20 yrs.	1941, etc.	0·68	+
C30	F.	27	1·57	M.S., A.I.	A.F.	150/104	III	5 yrs.	1950	0·63	++
C38	F.	33	1·52	M.S., M.I., A.I.	A.F.	150/85	II→III	11 yrs.	1949	0·71	+
C23	F.	55	1·52	M.S., A.I.	A.F.	160/80	III	38 yrs.	1943, 1948	0·71	+
C4	M.	21	1·55	M.S.	R.	110/70	III	1 yr.	Early failure O.A.	0·63	+
C31	F.	43	1·65	M.S., A.I.	A.F.	130/80	III	12 yrs.	1939, 1943	0·69	±

M.S.=Mitral Stenosis.
A.I.=Aortic Incompetence.
A.S.=Aortic Stenosis.
M.I.=Mitral Incompetence.
O.A.=On Admission.
R=Sinus Rhythm.
A.F.=Auricular Fibrillation.
J.V.P.=Jugular Venous Pressure.

in normal subjects, exercise causes no increase in the pulmonary artery pressure (Riley *et al.*, 1948; Cournand, 1950); or if it does, the rise is only slight (Dexter *et al.*, 1951). Thus in normals despite an increase in output with little or no change in intrathoracic blood volume, there is little change in the pulmonary artery pressure.

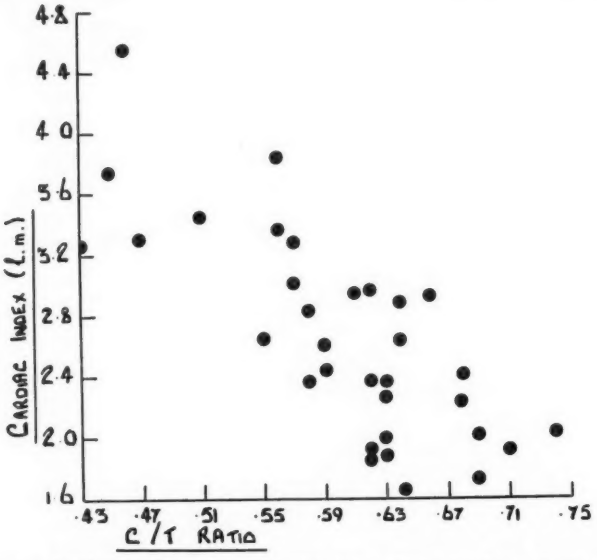

FIG. 3.—Resting cardiac index and heart size as shown by the cardiothoracic ratio in mitral stenosis. $r = -0{\cdot}78$; $P < 0{\cdot}001$.

The patients with mitral stenosis fall into two main groups—those with normal, and those with low cardiac outputs at rest. Despite differences in the output response, both groups usually show an increase in the intrathoracic blood volume on exercise, more constantly than the normal group. The rise in the low output group is less than in the normal output group, but the difference is not significant. Pulmonary artery or right ventricular pressures were only measured in seven of these cases and these were mainly in those with low outputs. All had a raised pressure at rest which increased further on exercise.

The rise in the intrathoracic blood volume on exercise may occur in any of its four compartments, as previously discussed. In mitral stenosis, especially in the low output group, the venous component might be expected to increase because of the rise in central venous pressure that usually occurs in this type of patient on exercise (Gorlin *et al.*, 1951; Bayliss *et al.*, 1950). It has been observed that patients with mitral stenosis in congestive failure with high central venous pressure show no significant increase in the intrathoracic blood volume (Kopelman and Lee, 1951), and it is unlikely that any slight increase in central venous pressure could cause much increase in this volume. Fig. 4 shows that although there is a close correlation between the central venous pressure and the intrathoracic blood volume in left ventricular failure, this is not so in mitral stenosis and the differences in the pulmonary vessels in these two conditions are probably accounted for. It would thus appear that increase in central venous pressure does not contribute much to the increase in intrathoracic blood volume that occurs on exercise in mitral stenosis. Delay in the dye reaching the heart was minimized by raising the arm above the head and massaging the vein immediately after the injection, and this would compensate for any reduction in venous return from the arm that might occur on leg exercise. It seems unlikely that an increase

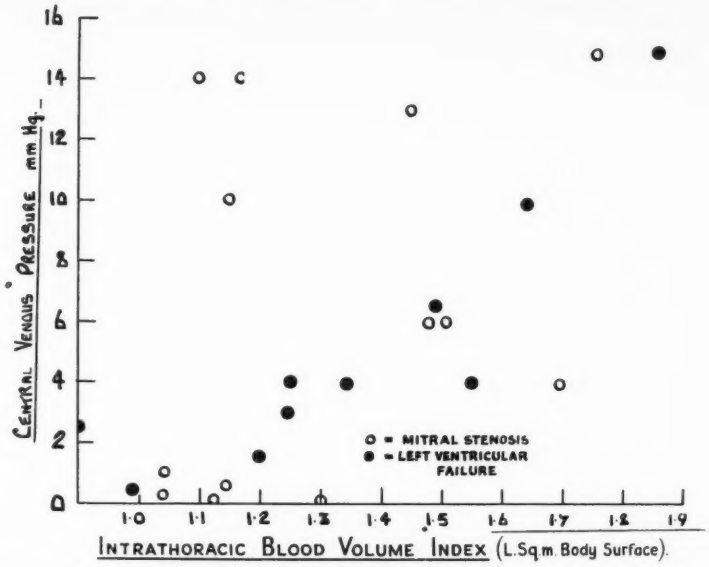

FIG. 4.—Central venous pressure and intrathoracic blood volume index in left ventricular failure and mitral stenosis.

in the aortic and arterial component could account for the rise, and therefore it is probable that the intrathoracic blood volume increase is contained either in the pulmonary vessels or the heart itself. Although no measurable change in the cardiothoracic ratio was observed in any patient on exercise, this does not exclude changes in the size of the left atrium which may enlarge posteriorly. The low output cases had the largest hearts and a small increase in size that hardly shows in the diameter may increase the volume considerably. The normal output cases mainly had smaller hearts and in these an increase of cardiac blood volume should have been more easily detected. The mean circulation time was shortened or unchanged in most cases on exercise, but, in four out of the five normal output cases who showed poor exercise response, this time was greatly prolonged. In the absence of much increase in heart size, this suggests some greater dilatation of the pulmonary vascular bed in these cases.

Hence it appears that the pulmonary blood volume in mitral stenosis may be normal or actually reduced at rest and the reduction when it occurs is probably in the smaller vessels. On exercise, in nearly all cases, there is an increase in the intrathoracic blood volume irrespective of functional capacity, resting cardiac output, or ability to raise the cardiac output. Some of this increase in volume may be in the pulmonary vessels, but the degree to which this occurs may vary in the different groups and the Hamilton dye method is not capable of showing this difference. However, among the patients with a normal cardiac output at rest, there were some with poor exercise responses but with an increase in the thoracic blood volume, accompanied by a prolongation in the mean circulation time; this may be due to a more labile vasculature capable of greater dilatation than the more severe cases.

SUMMARY AND CONCLUSIONS

The cardiac output, mean circulation time, and intrathoracic blood volume were measured at rest and during exercise by the Hamilton dye method in nine normal subjects and sixteen patients with mitral stenosis.

Normal subjects had a mean cardiac index of 3·3 litres at rest and most showed a rise on exercise, the mean being 4·3 litres per square metre. The intrathoracic blood volume was 1·2 litres per square metre at rest; it rose a little in some cases on exercise, but in others showed no significant change and in these the mean circulation time decreased on exercise.

Nine of the mitral stenosis patients had normal resting cardiac outputs with a mean cardiac index of 3·4 litres; the other seven had low cardiac outputs at rest with a mean of 2·2 litres per square metre. The intrathoracic blood volume in these groups was 1·16 litres and 1·22 litres per square metre and was not increased above the volume found in the normal group.

The significance of this is discussed and it is concluded that the pulmonary blood volume in mitral stenosis is normal or reduced when cardiac enlargement is present, and that this reduction takes place in the smaller pulmonary vessels. This is in contrast to the picture in left ventricular failure, where a rise in the pulmonary artery pressure is accompanied by an increased intrathoracic blood volume detectable by the same method.

On exercise the rise in the intrathoracic blood volume in mitral stenosis was approximately the same in both the normal and low output groups. However, other differences in the response to exercise were found in those with normal resting cardiac outputs, so that finally the patients with mitral stenosis could be separated into three groups.

Group 1. These patients had a normal resting cardiac output and mean circulation time and were able to raise their cardiac output to a normal level on mild exercise. The increase in the intrathoracic blood volume on exercise was more consistent than in normals.

These patients were only slightly incapacitated, and their hearts were only slightly, if at all, enlarged. Sinus rhythm was present and none had ever been in congestive failure.

Group 2. These showed only a small rise in cardiac output on exercise, although they had a normal resting output and mean circulation time. The increase in the intrathoracic blood volume on exercise was often accompanied by a prolongation in mean circulation time. This was not found in the other groups.

These patients were in Grade II to III functional capacity. Auricular fibrillation and cardiac enlargement were often present. A recent history of mild congestive failure with rapid recovery was common.

Group 3. A low cardiac output at rest was accompanied by a marked prolongation of the mean circulation time in these patients. On exercise, there was a poor response in cardiac output with a fall in stroke output, although most showed a rise in intrathoracic blood volume with the circulation time decreasing or remaining unchanged.

These patients were all fairly severely incapacitated. Auricular fibrillation was often present as well as gross cardiac enlargement. All had histories of congestive cardiac failure, some of long standing. In five of these patients, the pulmonary artery pressure was found to be greatly raised at rest, with further increase on exercise, although the intrathoracic blood volume was no greater than in the other groups.

The change in the intrathoracic blood volume on exercise does not help in differentiating pulmonary vascular changes of a more permanent nature. However, in this respect, the prolongation of the circulation time on exercise in the second group may indicate a more labile vasculature.

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INJECTION OF THE BRONCHIAL CIRCULATION IN A CASE OF TRANSPOSITION

BY

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Enlargement of the bronchial arteries in a case of pulmonary stenosis was first mentioned by Jacobson (1816). More recently East and Barnard (1938), Campbell and Gardner (1950), Grosse-Brockhoff *et al.* (1950), and Allanby *et al.* (1950) reported increases in the bronchial circulation in pulmonary atresia. In the experience of Taussig (1947), hypertrophy of the bronchial arteries is frequently seen in pulmonary stenosis and atresia and in persistent truncus arteriosus.

The present case concerns the combination of hypertrophied bronchial arteries with a patent, transposed pulmonary trunk, a right sided aorta, and a ventricular septal defect.

Case Report

The patient, a girl, aged 3, was admitted to the Children's Unit of Hammersmith Hospital under the care of Dr. Mann. She became blue on the sixth day after birth and squatted all her life. Her fingers and toes were clubbed and a soft systolic murmur, loudest at the tricuspid area, was conducted posteriorly and was audible along the medial border of the left scapula. This suggested enlargement of the bronchial arteries as emphasized by Campbell and Gardner (1950). The blood pressure was 100/60: the hæmoglobin, 25·6 g. per 100 ml.; red blood corpuscles 9·9 millions. The cardiogram showed right ventricular preponderance. On screening, the lung fields seemed oligæmic (Fig. 1) and the pulmonary arteries were difficult to identify.

A Blalock operation was performed by Mr. W. P. Cleland. The pulmonary artery pressure was thought to be reduced, and the left subclavian artery was inserted into the left pulmonary artery. On releasing the clamp from the pulmonary artery, the colour of the child changed to pink. Twenty hours later, sudden dyspnœa and cyanosis developed, and the child succumbed to pulmonary œdema.

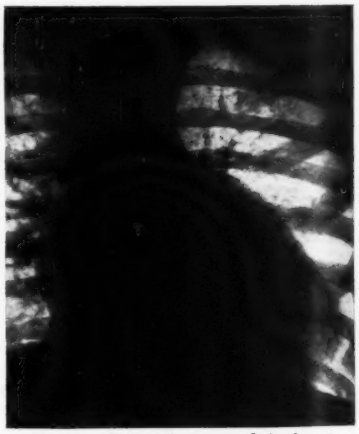

FIG. 1.—Teleradiogram of the heart and lung fields.

Post-mortem findings. The body of the child was undersized. The chest and abdomen were opened and the veins everywhere showed engorgement. The kidneys and liver were enlarged, but the spleen was of normal size. No fluid or adhesions were present in the pleural sacs and the lungs were œdematous. The heart lay in a horizontal position and was hypertrophied. The aorta arose from the anterior (right) ventricle, and two normal sized pulmonary arteries emerged from behind the aorta. The pulmonary trunk came from the posterior (left) ventricle. The left subclavian

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Fig. 2.—Radiograph of injected thoracic contents viewed in an antero-posterior position. (A) Heart. (B) Left and (BB) right coronary artery. (C) Right pulmonary artery. (D) Left subclavian anastomosis. (E) Ligature around descending thoracic aorta (EE) Descending aorta. (F) Left bronchial arteries. (G) Right bronchial artery. (I) Pulmonary artery bed. One-third of normal size.

anastomosis was secure and no leakage was evident. The total thoracic content was then removed in bulk.

Anatomical findings after injection. The descending aorta was firmly clamped beyond the origin of the left subclavian artery, and a cannula introduced into the distal end of the descending thoracic aorta. The technique of the injection of the bronchial arteries and the radio-opaque medium used were the same as described by Cudkowicz and Armstrong (1951). The medium does not penetrate vessels of less than 60 μ in diameter.

Following the injection, the heart was opened. A minute hole between the atria could be demonstrated. A large ventricular septal defect was present in the middle third of the septum. Both ventricular muscles were hypertrophied, and one cusp of the pulmonary valve was deformed and thickened: this could have caused some obstruction to the outflow. The ductus arteriosus was not patent. The bronchial arteries were followed from the hila along the main bronchi of each lung, and evidence of direct communication between the trunks of the bronchial and pulmonary arteries could not be found. A network of very fine arterioles, filled with the injection medium, was noted to course across the adventitia of the pulmonary arteries. It was thought that these vessels were dilated vasa vasorum which are normally derived from the bronchial arteries (Miller, 1947).

Radiography. The radiographs of the injected thoracic content, taken before the heart was opened, showed that three large bronchial arteries entered the left lung hilum after emerging from the lateral aspect of the descending aorta. A large branch derived from the uppermost of the three arteries crossed the aorta posteriorly and entered the right hilum. A fourth bronchial artery arising immediately below the other three coursed directly from the aorta to the right hilum. The intrapulmonary course of the vessels became lost because of the complete superimposition of the pulmonary arterial trees, which had filled indirectly through the bronchial arteries. The injection medium, which had traversed intrapulmonary anastomoses to reach the pulmonary arteries, was conveyed to the ascending aorta and its branches through the patent subclavian anastomosis (see Fig. 2).

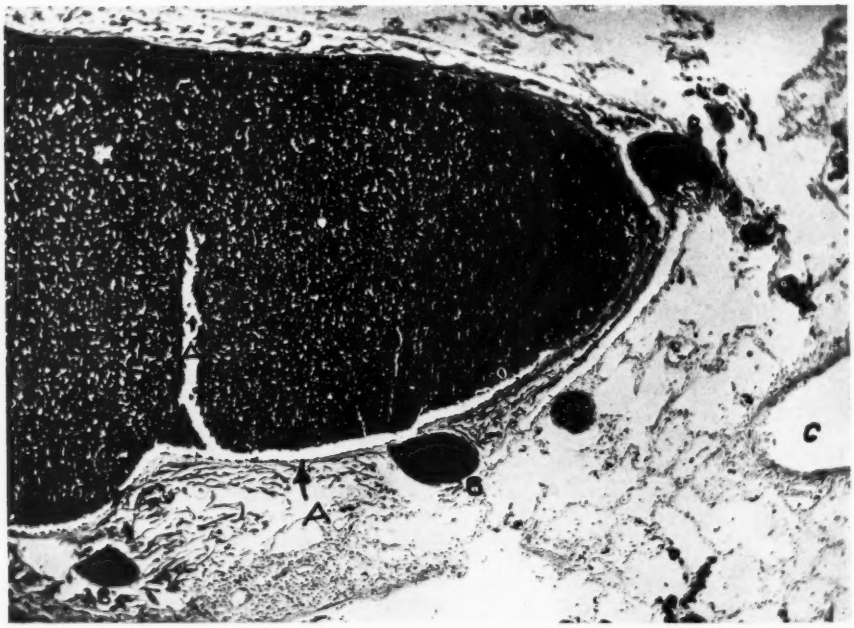

FIG. 3.—Photomicrograph of an intrapulmonary branch of a pulmonary artery approximately two inches from the left hilum. (A) Dilated pulmonary artery filled with bismuth granules. (B) Densely filled vasa vasorum in the adventitia. (C) Empty pulmonary vein. (Magnification, ×75)

Histology and serial sections. The injection medium fixed well and allowed the injected vessels to be traced histologically. The medium appeared as a mass of black granules in vessels of more than 60 μ in diameter.

Cuts were examined along broncho-vascular bundles from the hila to the periphery. These showed no alteration in the pattern of the bronchial arteries to the various intrapulmonary structures which they normally supply. The walls of the bronchi were unchanged, and normal-sized bronchial arterioles were visible in the mucosa, substantia propria, and near the cartilages. The pulmonary arteries accompanying these bronchi were also well injected, but less densely. The walls of the pulmonary arteries appeared thinner than normal and many dilated vasa vasorum in the adventitia communicated freely with their lumina (see Fig. 3 and 4). Sections from the lung periphery showed filling of all intrapulmonary arterioles, but those normally derived from the bronchial arteries,

such as interlobular septal or pleural arterioles, were more densely filled. The pulmonary veins and capillaries remained uninjected throughout, because of the inability of the injection medium to penetrate vessels less than 60 μ in diameter.

FIG. 4.—Photomicrograph of pulmonary arteriole in the lung periphery. (A) Dilated and injected pulmonary arteriole. (B) Dilated communicating and densely injected vas. (C) Accompanying small bronchi. (Magnification, ×35.)

DISCUSSION

The post-mortem radiographical and histological study of the injected bronchial circulation in this case suggests that bronchial artery hypertrophy occurred in the presence of patent pulmonary arteries, although some reduction in total pulmonary artery blood flow may have been caused by the deformed cusp of the pulmonary valve. A considerable volume of deoxygenated blood reached the pulmonary capillaries from the right sided aorta through the bronchial arteries, and this was conveyed to the pulmonary arteries as a result of the enlargement and direct anastomoses of the vasa vasorum with the pulmonary artery lumina. No evidence of direct shunts between the trunks of the bronchial and pulmonary arteries could be seen, and the distribution of the bronchial arteries within those intrapulmonary structures that they normally supply was unaltered. The pre-capillary anastomoses between the two circulations appear, therefore, to have been brought about by the dilatation and penetration of the vasa vasorum which are normally present in the adventitia and media of the pulmonary arteries. Augmented bronchial blood flow has been thought to follow obstruction to the pulmonary arteries, (Virchow, 1856; Taussig, 1947). Karsner and Ash (1912) believed that diminution in pulmonary artery pressure alone could also increase the flow through the bronchial arteries: the mechanism of the readjustment is not known. In histological studies of injected bronchial arteries in tuberculosis, certain types of pulmonary emphysema, lung neoplasms, and bronchiectasis where thrombosis of the pulmonary arteries was apparent, recanalization of the occluded lumina by vigorously proliferating vasa vasorum was demonstrable (Cudkowicz, 1951). It would appear, therefore, that these small branches of the bronchial arteries, which do not normally communicate directly with the lumina of the pulmonary arteries (Miller, 1947), can in the presence of diminished pulmonary artery blood flow or pul-

monary artery occlusion effect pre-capillary anastomoses, which in turn become associated with hypertrophy of the bronchial arteries. The presence of enlarged bronchial arteries in congenital heart diseases associated with patent pulmonary arteries suggest that the pulmonary vascular capacity is already utilized to its maximum, and this may very well constitute a contra-indication for further operative augmentation of pulmonary blood flow.

Summary

The bronchial circulation was studied at necropsy in a case of transposition of the great vessels with ventricular septal defect and closed ductus arteriosus. Enlargement of the bronchial arteries and direct wide-spread pre-capillary anastomoses by dilated vasa vasorum with the pulmonary arteries was demonstrated. The significance of these findings in regard to further surgical augmentation of pulmonary blood flow is discussed.

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THE ELECTROCARDIOGRAPHIC FEATURES OF HIGH POSTEROLATERAL MYOCARDIAL INFARCTION

BY

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The cardiographic features of anterior and posterior myocardial infarction are well recognized. The occurrence of high lateral infarction has also been established, but infarction confined to the posterolateral aspect of the heart has in contrast received little attention. It is the purpose of this paper to stress the diagnostic cardiographic features of infarction in this area.

Anatomically the heart is an irregular and slightly flattened cone, with a base, an apex, and three surfaces, described anatomically as the sterno-costal, the diaphragmatic, and the left. Cardiographically, lesions of the sterno-costal and diaphragmatic surfaces are classified respectively as anterior and posterior. The left surface faces backwards, upwards, and to the left. It is not in close relationship to any of the six routine præcordial leads, but does in part face towards the left shoulder. Infarction confined to this left surface is posterolateral in position. As there is no lesion of the diaphragmatic surface, the infarct should be classed cardiographically as a " high " posterolateral infarct.

In 1944 Wilson pointed out that the combination of diagnostic changes of infarction in the left leg lead, unusual prominence of the R and T waves in leads to the right of the præcordium, and significant abnormalities in leads V5 and V6, was associated with infarction of the posterolateral aspect of the heart. Myers *et al.* (1949) have reported on 33 cases which at autopsy showed infarction of the posterolateral aspect, and have correlated the cardiographic and post-mortem findings. Changes in the left leg lead were taken as an index of the posterior aspect of the lesion, while the lateral extension was evidenced by præcordial leads V5 and V6 and the left arm lead. Less than one-third of the cases showed diagnostic changes in both limb leads. In the majority of cases changes of infarction were confined to one or other limb lead, depending on the exact size and position of the infarcted area, and on the position of the heart, particularly the degree of rotation around the long axis. Two cases showed no evidence of infarction in either limb lead. Sixteen cases were observed during the acute stage, and in eleven, præcordial leads from V1 to V4 showed reciprocal depression of the S–T segment, or exaggeration of the height of the R and T waves or of the T waves alone, sufficient to arouse suspicion of posterolateral infarction. Both Wilson and Myers have illustrated their writings, but in no record does the R wave exceed the S wave in V1. Sears and Myers (1950) now record additional leads from the back of the chest in these cases, but have not as yet published their results. Recently Levy (1950) has stressed the occurrence of a prominent R wave and shallow S wave in lead V1 in lateral infarction; in eight of his twelve cases, the infarct was localized to the posterolateral aspect, but autopsy confirmation was apparently not available.

Material

Thirteen patients, four of whom have been followed to necropsy, provide the material for this paper. In all cases, the standard leads, unipolar limb leads, and præcordial leads V1 to V6 were recorded. Additional leads taken from points in the interspaces vertically above V4 to V6 were

obtained in seven cases; while in six leads were also taken from the back of the chest. Leads V7, V8, and V9 were recorded from the left side of the chest, at the posterior axillary line (V7), subscapular line (V8), and paravertebral line (V9) respectively, at the same horizontal level as leads V4 to V6 (i.e. the horizontal level of the fifth left interspace at its junction with the mid-clavicular line). High leads on the back of the chest were taken from points vertically above V7 to V9, at the horizontal level of the third interspace at its junction with the sternum. In the normal healthy person, leads V7 to V9 show an upright P wave, a small narrow Q wave, a moderate R wave, and an upright T wave. The higher leads taken above V7 to V9 are of similar form but are of lower voltage. Fig. 1 illustrates the tracings obtained from a healthy person in whom the heart was vertical in position. In posterior infarction, where the lesion is confined to the diaphragmatic surface, these additional leads are also of normal form.

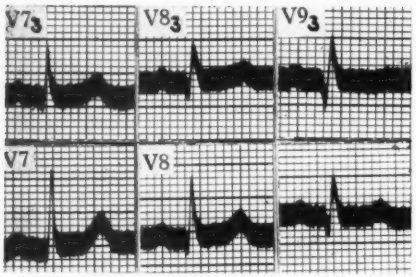

FIG. 1.—The records illustrate the normal form of complex in leads taken from points on the back of the chest in the left posterior axillary line, scapular line, and paravertebral line, (1) at the same horizontal level as the routine præcordial leads (V7, V8, and V9 respectively) and (2) at the horizontal level of the third interspace at its junction with the sternum (V73, V83, and V93 respectively). The heart was vertical in position.

The first patient, whose initial record is illustrated in Fig. 2, was originally diagnosed as having sustained a high lateral infarct, but the additional leads taken in the first, second, third, and fourth interspaces vertically above V4 to V6 were within normal limits. The presence of S–T depression in V4 and V5 in the original record, and the subsequent development of a tall R wave in V1 and high upright T waves in the præcordial leads, suggested that the infarct was on the posterior surface, and was in fact posterolateral in position. At autopsy, three months after the acute attack, a large healed infarct, oval in shape, 5×7 cm. in size, and involving the full thickness of the left ventricular muscle, was demonstrated on the posterolateral aspect.

The record shown in Fig. 3 was obtained 5 days after a coronary thrombosis in a man, aged 52 years. The standard and unipolar limb leads show changes that, classically, are associated with infarction of the anterior surface of the heart, but the præcordial leads V1 to V6 show no certain evidence of anterior infarction. High leads taken from the interspaces above V4 to V6 also failed to demonstrate dead muscle. Inspection of the præcordial leads does reveal certain unusual features—the tall R wave in V1, the relatively deep S wave in V6, the absence of a definite transitional zone, the high upright T waves in V2 and V3, and the slight S–T elevation with low upright T waves in V5 and V6. Serial records (Fig. 4) revealed changes typical of infarction in the left arm lead and in standard lead I; persistence of the predominance of R in V1, and the deep S wave in V6; reduction in the height of the T waves in V2 and V3; and development of T wave changes suggestive of underlying muscle damage in V5 and V6. Leads taken from the back of the chest revealed the typical serial changes of recent underlying myocardial infarction (Fig. 5). In the record illustrated, leads V7 and V8 are overlying the edge of the infarct, but in the leads taken above V7 and V8, in the horizontal level of the 3rd interspace at its junction with the sternum, the initial deflections consist of a small broad Q wave, and a small R wave, with, in the first record, elevation of the S–T segment; and, in subsequent records, inversion of the T wave of coronary type. The P waves in these leads are upright, showing that the electrodes do in fact face ventricular muscle, and not the back of the heart.

Three other cases showed this general pattern in the twelve leads routinely recorded, and additional leads from the back of the chest revealed the infarcted area. Four further cases were different in that the initial deflections in the præcordial leads were within normal limits (Fig. 6). All showed abnormally high T waves in two or more of the præcordial leads, and in two cases

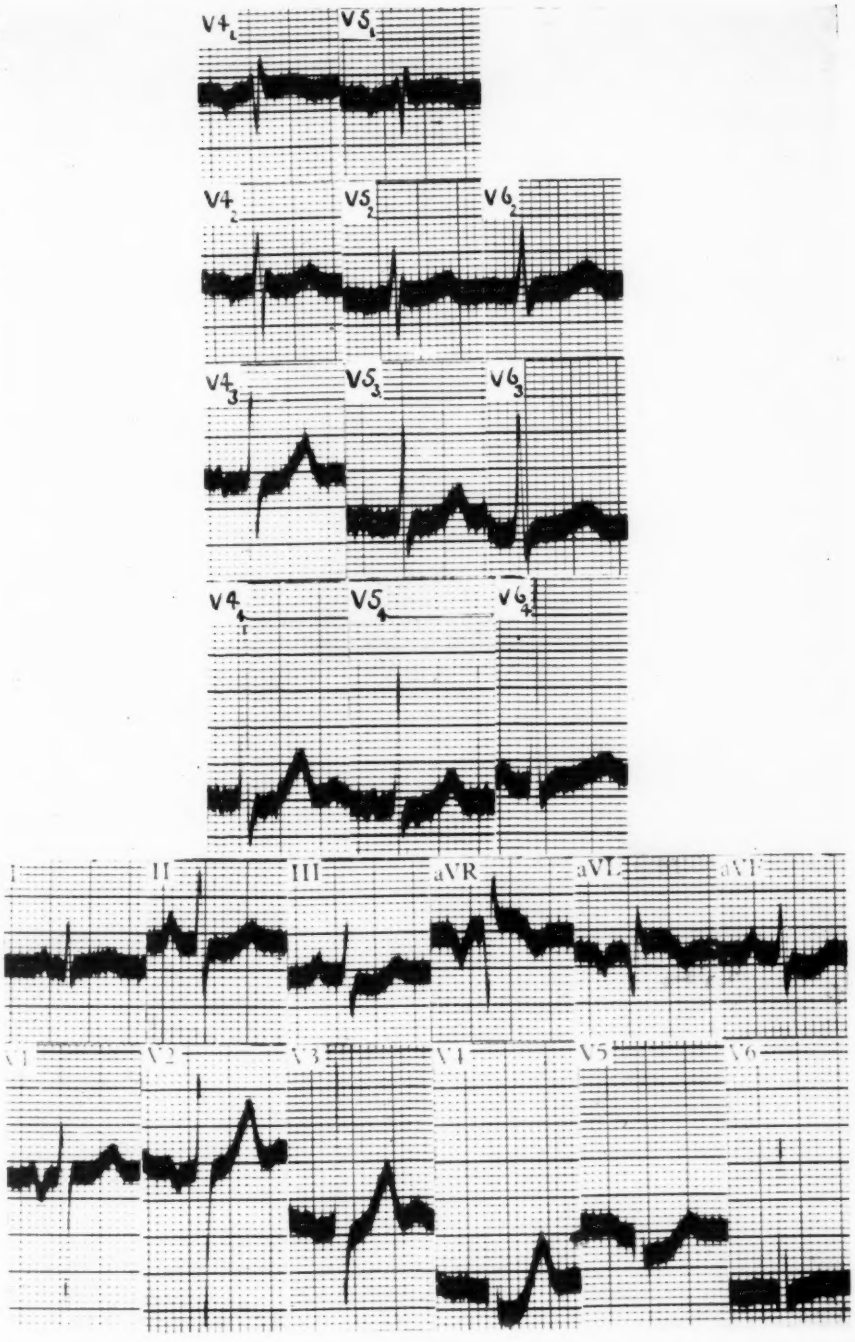

FIG. 2.—Cardiogram of Case 1 showing evidence of high lateral infarction in the unipolar limb leads. The additional leads taken from the first, second, third, and fourth interspaces vertically above V4, V5, and V6 fail to reveal underlying damaged muscle.

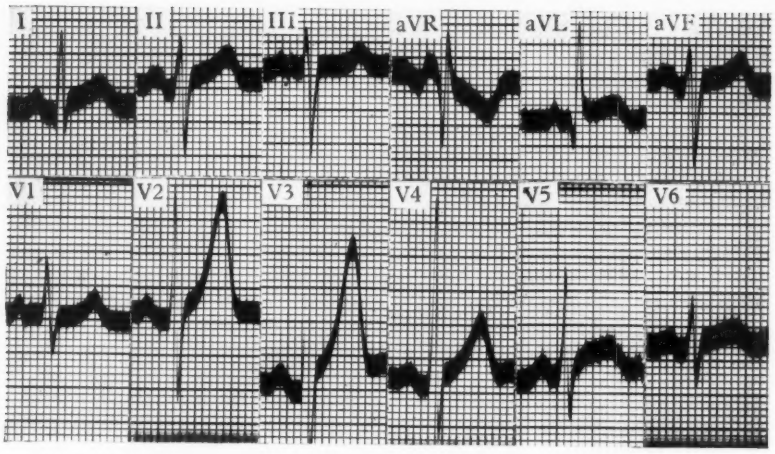

FIG. 3.—Cardiogram taken 5 days after a coronary thrombosis in Case 2.

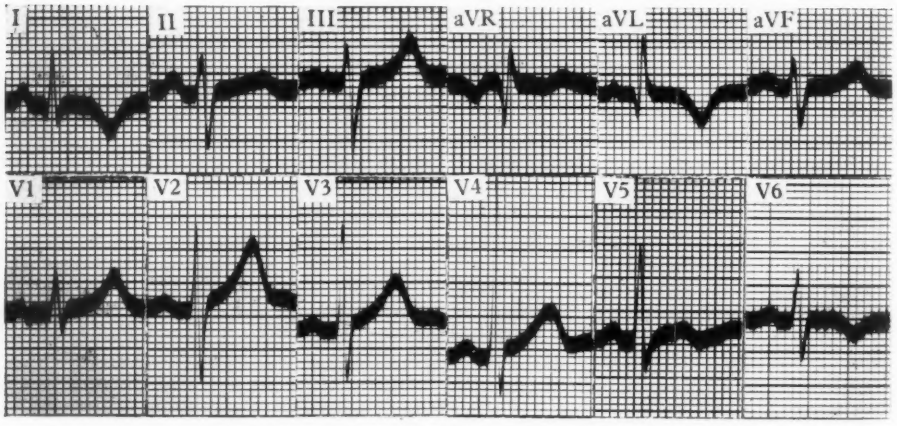

FIG. 4.—Cardiogram taken 27 days after the coronary thrombosis in Case 2.

there was also S–T depression in the acute stage. Changes suggestive of infarction were present in the left arm lead and in standard lead I.

The remaining four cases showed a slightly different pattern, but the changes, once recognized, were equally diagnostic. The record illustrated in Fig. 7A was obtained six weeks prior to the development of a coronary thrombosis in a male, aged 55 years, who had reported with symptoms of left ventricular failure and had well marked hypertension. It shows evidence of left ventricular hypertrophy. Fig. 7B was recorded five days after a clinical coronary thrombosis in this patient. There was no definite cardiographic evidence of myocardial infarction, but the reduction in the height of the R wave in the left arm lead and in standard lead I, coupled with the S–T depression in V4 to V6 suggested the presence of diffuse subendocardial necrosis in the left ventricle. Necropsy after 19 days showed a transmural infarct on the posterolateral aspect of the left ventricle, extending in a strip just over one inch wide from near the auriculoventricular sulcus to just above the

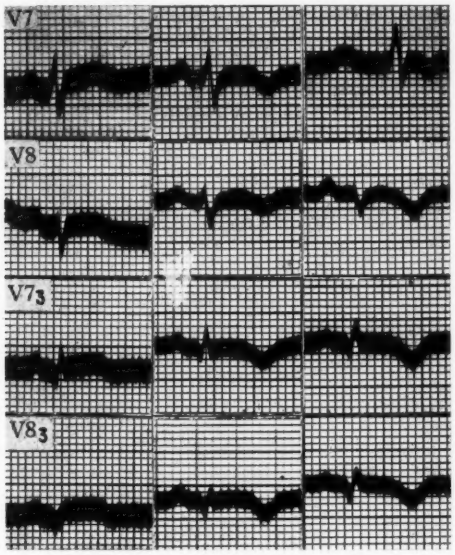

FIG. 5.—Records taken from the back of the chest in Case 2, at 5, 19 and 27 days after the coronary thrombosis. The electrodes were placed in the manner described in Fig. 1.

apex (Fig. 8). A considerable mass of hypertrophied left ventricle remained between the infarct and the posterior edge of the interventricular septum. Two other patients in whom the cardiogram showed essentially similar features have since been observed. In each the diagnosis was confirmed at necropsy, a strip of infarcted muscle being demonstrated on the posterolateral aspect of the left ventricle. The fourth case differed slightly in that there was no associated cardiographic evidence of left ventricular hypertrophy and was some S–T depression in the præcordial leads, mainly

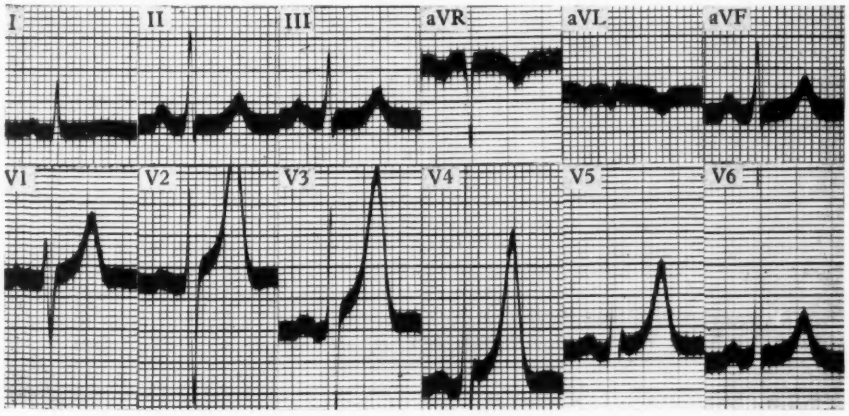

FIG. 6.—Cardiogram showing abnormal high T waves in the præcordial leads, with no QRS changes.

in V1 to V4. Serial leads taken from the back of the chest in this patient (from the points previously described), showed S–T and T wave changes diagnostic of underlying infarction.

Discussion

The left shoulder faces both the sterno-costal and left surfaces of the heart. Infarction high on either surface and lateral in position may therefore be detected in the left arm lead. Should additional leads taken from the intercostal spaces above V4 to V6 prove normal in such a case, then leads taken above V7 and V8 will reveal underlying muscle damage. It is suggested that the following five features occurring in the twelve leads routinely recorded (3 standard limb leads, 6 unipolar præcordial leads, and 3 unipolar limb leads) constitute one pattern of high posterolateral myocardial infarction—(1) evidence of infarction in the left arm lead, and so in standard lead I;

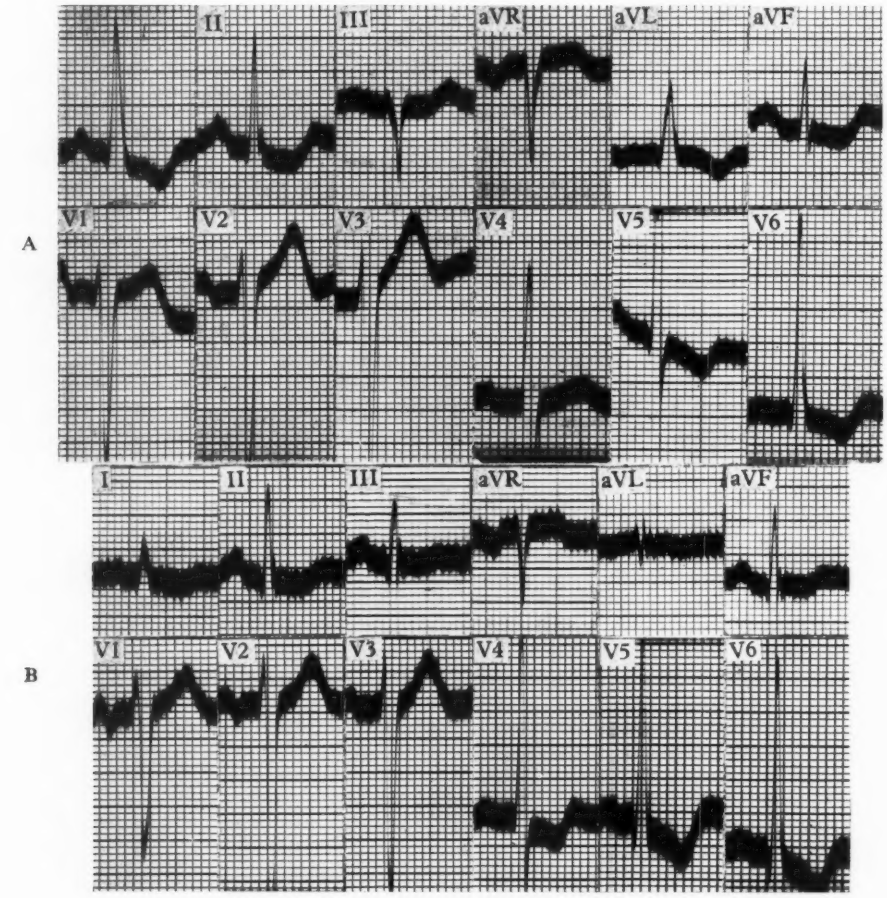

Fig. 7.—(A) Cardiogram of Case 10 recorded six weeks before the myocardial infarct showing evidence of left ventricular hypertrophy; (B) Cardiogram obtained 5 days after a clinical coronary thrombosis in this patient.

(2) a predominant R wave in V1; (3) absence of a definite transitional zone in the præcordial leads; (4) high T waves in two or more of the præcordial leads; and (5) in the acute stage, S–T depression in the præcordial leads. The depth of the S wave in V6 may be helpful, but in some cases this S wave is not abnormal. Chest leads V5 and V6 commonly overlie the edge of the infarcted area.

The tall R wave in V1 and the deep S wave in V6 (Fig. 3 and 4) are probably due to relative predominance of the right ventricle. This could occur in a previously normal heart were the left ventricular muscle on the back of the heart damaged. Serial records taken from the back of the chest in the horizontal levels of the fifth and third interspaces anteriorly should overlie and demonstrate the infarcted area, and in fact do so (Fig. 5).

FIG. 8.—Serial sections of the heart in Case 10 showing the left ventricular hypertrophy and the strip of infarcted muscle on the posterolateral aspect.

As might be expected, the exact size and position of the infarcted area, the position of the heart and the form of the cardiogram prior to the development of the infarct, are important in determining the changes resulting from infarction. As stated, five of the cases showed the pattern just described. In these, the heart was horizontal or intermediate in position. Forward rotation of the apex may, without changing the præcordial lead pattern, alter the form of the leads from the left arm and the left leg, bringing the diagnostic changes of infarction into the left leg lead. This occurred temporarily in one case. In no other case did the left leg lead show diagnostic changes of infarction, indicating that the diaphragmatic surface of the heart was intact. In each of the four cases showing no abnormality of the initial deflections in the præcordial leads the heart was electrically vertical or intermediate in position. The normal form of the initial deflections in the præcordial leads may indicate that the area of infarction is small, and that there is an adequate mass of left ventricular muscle opposing the right ventricle. This contention is supported by the findings at necropsy in the three cases showing cardiographic evidence of left ventricular hypertrophy, one of which is illustrated in Fig. 7 and 8. In these cases the left ventricle was grossly hypertrophied, and the area of infarction was long and narrow with a mass of hypertrophied muscle behind it. After the

development of the infarct, the cardiographic evidence of left ventricular hypertrophy therefore tends to persist in præcordial leads V1 to V6, and to distort and obscure the changes produced by muscle damage and death on the posterolateral aspect. In such cases the features suggestive of high posterolateral infarction are (1) the presence in the præcordial leads V1 to V6 of normal initial deflections, or of increase in the depth of the S wave in V1 and V2 and in the height of the R wave in V5 and V6, due to the left ventricular hypertrophy; (2) S–T depression in the præcordial leads, which, if there are S–T and T wave changes of left ventricular hypertrophy, occurs in leads further to the right than would be expected if left ventricular hypertrophy alone were present; (3) presence of a small and sometimes bifid R wave in the left arm lead and standard lead I, out of keeping with the height of the R waves in V5 and V6, and associated with a flat or inverted T wave. The T waves in V2 and V3 may not be abnormally tall. In the absence of left ventricular hypertrophy inversion of the T wave of " coronary type " may develop in V5 and V6.

Not only may the evidence of posterolateral infarction be suppressed by the presence of left ventricular hypertrophy, but it is possible that, some days or weeks after the infarct has been sustained, the pattern of infarction in the left arm lead may be mistaken for that of left ventricular hypertrophy. Attention to the breadth of the Q wave, the relative height of the R wave, and the symmetrical inversion of the T wave, should minimize such difficulties (Goldberger, 1949).

Conclusions

Infarction of the anatomical left surface of the heart—high posterolateral infarction—produces characteristic changes in the twelve cardiographic leads routinely recorded, when the infarct is of sufficient size. These changes are: (1) diagnostic signs of infarction in the left arm lead, and in standard lead I; (2) a predominant R wave in V1; (3) absence of a definite transitional zone in the præcordial leads; (4) high upright T waves in two or more of the præcordial leads; and (5) in the acute stage, S–T depression in the præcordial leads. Leads V5 and V6 commonly overlie the edge of the infarct. Additional leads taken from the back of the chest demonstrate the infarcted area. The position of the heart, the size of the infarct, and the preceding cardiographic pattern, are all important in determining whether the full picture described above appears in the præcordial leads, or whether only S–T and T wave changes develop. In the presence of much left ventricular hypertrophy the following changes are associated with the occurrence of a high posterolateral infarct—(1) S–T depression in the præcordial leads, further to the right than found with left ventricular hypertrophy alone, and (2) reduction in the height of the R wave in the left arm lead and standard lead I, out of keeping with the height of R in V5 and V6, and possible splintering of this small R wave. The T waves in the left arm lead and standard lead I remain inverted, or become inverted, while in præcordial leads V2 and V3, abnormal high T waves may not develop.

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TRICUSPID ATRESIA: A NEW RADIOSCOPIC SIGN

BY

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The object of this paper is to call attention to a radioscopic sign recently observed in two cases of tricuspid atresia. To the best of the writer's knowledge, this has not been previously noted, and it would appear to be of value in establishing the diagnosis before more elaborate investigations are carried out.

The sign consists of the asynchronous pulsation of the anterior and posterior cardiac borders when viewed in the left (II) oblique position. In the normal heart, contraction is synchronous, the posterior border being formed by left ventricle and the anterior border by right ventricle, though occasionally, particularly if an insufficient degree of rotation is employed, the upper part of the anterior border may be formed by the right auricle. Whilst screening a child with cyanotic congenital heart disease it was observed that in the left (II) oblique position, the posterior cardiac border contracted appreciably after the anterior. At the time it was thought that this finding might have been due to either (1) left bundle branch block, or (2) replacement of the right ventricle as the main component of the anterior border by the right auricle, as would occur in tricuspid atresia when the right ventricle is non-functioning and hypoplastic. Since left bundle branch block had already been excluded by a full cardiogram, the latter hypothesis was accepted as the more likely. The diagnosis of tricuspid atresia was subsequently proved by angiocardiography.

Another child with tricuspid atresia and presystolic contraction of the anterior heart border has since come under observation.

In practice, the theoretical concept that a similar appearance might be produced by bundle branch block has not been borne out. Numerous cases of both left and right bundle branch block have since been screened and no asynchrony of ventricular contraction has been detected. Nor has this phenomenon been observed in any other condition with the exception of one case in which the diagnosis of tricuspid atresia although possible, was not proved.

Case Reports

Case 1. Aged 8. Permanent cyanosis had been present from birth. The exercise tolerance was poor and squatting frequent. Deep cyanosis was present, the fingers and toes were clubbed, and the left ear was deformed. The height was 50 in. and the weight 42 lb. (average normal values 50·7 in. and 58·3 lb. (O'Brian *et al.*, 1947). The blood pressure was 90/70. The heart was enlarged to the left and soft systolic murmurs were present at the apex and base. The second sound was slightly accentuated in the second left interspace. The hæmoglobin was 162 per cent. A cardiogram (Fig. 1) showed abnormal left axis deviation (−40°). The præcordial leads were unusual but suggestive of left ventricular enlargement. X-ray examination (Fig. 2) showed that the cardiac enlargement was due almost entirely to the left ventricle. The left auricle and right side of the heart appeared normal. On radioscopy in the left (II) oblique position the anterior border, which was of apparently normal contour was seen to contract appreciably before the posterior which was formed by the enlarged left ventricle. It is suggested that this was due to replacement of the right ventricle as the main component of the anterior border by the right auricle as the result of right auricular enlargement combined with hypoplasia of the right ventricle. It is interesting to note that the

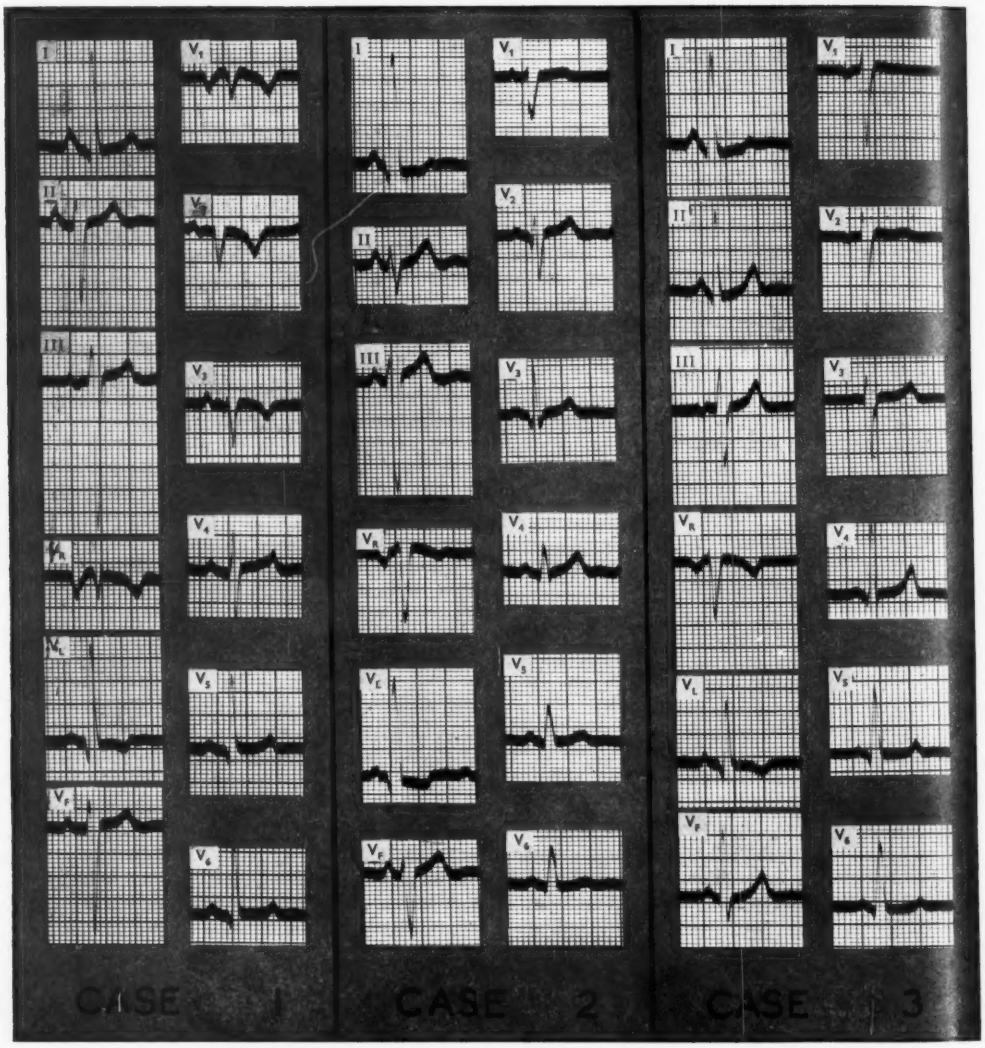

FIG. 1.—Cardiograms of three cases of tricuspid artresia described in the text.

radiologist commented on the normal appearance of the right side of the heart in the left oblique view. Angiocardiography demonstrated a large communication between the right and left auricles, absence of filling of the right ventricle and filling of the aorta at 2½ seconds. These findings were considered diagnostic of tricuspid atresia. Operation was refused.

Case 2. Aged 8. Permanent cyanosis had been present from birth. The exercise tolerance was poor, minimal exertion producing severe dyspnœa. Deep cyanosis was present and the fingers and toes were clubbed. The height was 48 in. and the weight 40 lb. (average normal values 50·3 in. and 57·1 lb.). The blood pressure was 110/90. A harsh systolic murmur was audible over a fairly wide area, maximal over

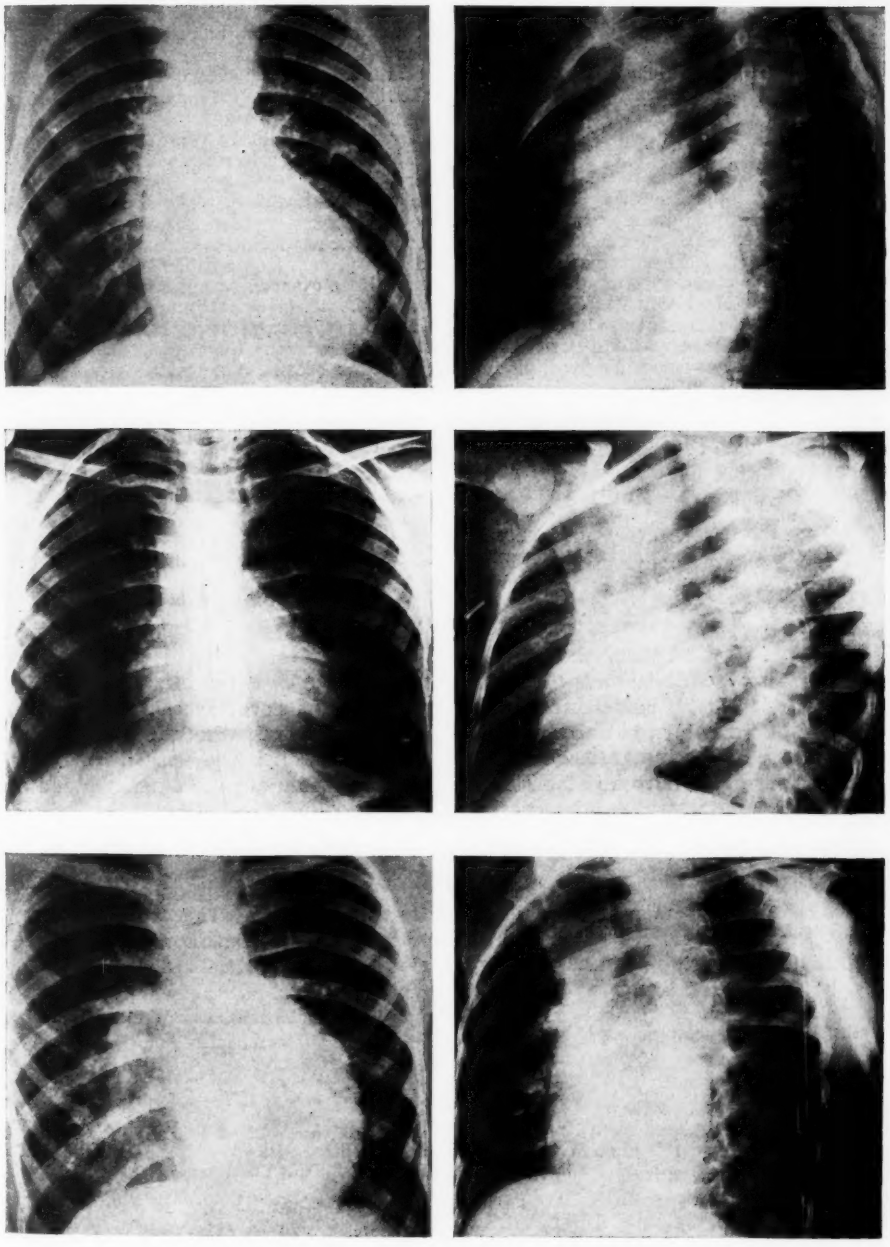

FIG. 2.—Postero-anterior and left (II) oblique radiographs of Cases 1, 2, and 3.

the sternum opposite the third and fourth interspaces. The hæmoglobin was 134 per cent. A full cardiogram (Fig. 1) showed borderline abnormal left axis deviation (−30°) and left ventricular enlargement. The X-ray films (Fig. 2) revealed no radiological cardiac abnormality. On radioscopy, although the heart was normal in size and shape, presystolic pulsation of the right border was seen in the P-A view, and of the anterior border in the left oblique position. An angiocardiogram demonstrated a large communication between the right and left auricles, absence of filling of the right ventricle, and filling of the right sided aorta at 1½ seconds.

These findings were considered diagnostic of tricuspid atresia. In this case, prior to angiocardiography, the diagnosis was in doubt owing to the normality of the radiological appearances. The radioscopic findings, however, lent support to the diagnosis of tricuspid atresia.

A Blalock-Taussig operation was performed from which the patient made a good recovery. Owing to her condition at the time, however, exploration to verify the diagnosis was considered inadvisable.

The sign described has also been observed in the following case in which the diagnosis remains in doubt.

Case 3. Aged 14. Intense permanent cyanosis had been present from birth. The exercise tolerance was much limited by severe dyspnœa on minimal exertion. Deep cyanosis was present and the fingers and toes were clubbed. The height was 60·5 in. and the weight 79 lb. (average normal values 61·2 in. and 106·2 lb.). The blood pressure was 110/60. When first seen in 1947, a basal systolic thrill and a loud systolic murmur, maximal in the second and third left interspaces were present. Since then, this patient's condition has improved somewhat, while the thrill and murmur have become more pronounced. The hæmoglobin was 138 per cent and a cardiogram (Fig. 1) showed left ventricular enlargement with an electrical axis of 0°. X-ray films (Fig. 2) showed an unusual cardiac outline with an absence of projection of the heart border to the right. Nevertheless, the transverse diameter was at the upper limit of normal. In the left (II) oblique view, the left ventricle was seen to be enlarged; the anterior border of the heart showed no abnormality, but radioscopy revealed presystolic contraction of the anterior border. Angiocardiography demonstrated a large communication between the right and left auricles and absence of filling of the right ventricle.

The film at 2 seconds was unexposed and at 3 seconds both aorta and pulmonary artery were filled.

The evidence afforded was thus consistent with a diagnosis of tricuspid atresia, but this was not proved.

Discussion

The principal signs on which the diagnosis of tricuspid atresia rests are permanent cyanosis associated with left axis deviation in the cardiogram, but the latter is not invariably present (Ash, 1950 and Taussig, 1947), nor is radiography always helpful, since the cardiac outline is not always typical and may even be normal. While, in the majority of patients, the diagnosis may be fairly straightforward, there are some in whom it is uncertain; it is suggested that the sign described above may be of value in establishing the diagnosis when angiocardiography and cardiac catheterization are not immediately practicable.

Summary

What is believed to be a new sign of tricuspid atresia is described. This consists of presystolic pulsation of the anterior cardiac border in the left oblique position. Details of two established and one doubtful case of tricuspid atresia showing this sign are given.

I wish to thank Professor Crighton Bramwell for his permission to publish details of these cases, and for his greatly valued help and encouragement.

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ELECTROCARDIOGRAPHIC CHANGES IN ACUTE POLIOMYELITIS IN CHILDHOOD

BY

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The early pathological accounts of poliomyelitis were limited to descriptions of the changes in the neuraxis. Wickman (1907) in his classical monograph on the disease alluded to the common occurrence of lymphoid hyperplasia, as did Harbitz and Scheel (1907), and Peabody *et al.* (1912), but none of these writers mentioned myocardial lesions. Robertson and Chesley (1910) observed swelling of myocardial fibres accompanied by interstitial œdema in 4 of 6 patients dying from poliomyelitis: this appears to be the first mention of myocardial damage in poliomyelitis. In 1918, Abramson described perivascular collections of mononuclear cells in the connective tissue septa between normal muscle bundles. Further brief descriptions of myocardial lesions were given by Cowie *et al.* (1934) and Clark (1938). Saphir and Wile (1942) noted myocardial changes in 6 of 7 patients dying early in the disease; five of these patients were children between 4 and 14 years old; one was 23, and one 34. They described foci of infiltration with lymphocytes and polymorphonuclear leucocytes around vessels in the myocardium and, in some cases, monocytes and adventitial cells were also present; the muscle fibres showed only minimal degenerative changes.

Further reports on the myocardial lesions have been made by Peale and Lucchesi (1943), Dublin and Larson (1943), Saphir (1945), Gefter *et al.* (1947), Dolgopol and Cragan (1948), Ludden and Edwards (1949), and Spain *et al.* (1950). Detailed reports on single cases have been given by Hassin (1943), Boucek *et al.* (1949), and Baskin *et al.* (1950). It is of interest that similar cardiac findings have been described in infective polyneuritis by Sabin and Aring (1941).

The incidence of myocardial damage detected in poliomyelitis varies widely. This may be due to the thoroughness of examination for if the whole heart is examined microscopically more lesions will be revealed than when only a few sections are examined. It is also possible that the incidence of cardiac damage varies in different epidemics (Spain *et al.*, 1950).

TABLE I

INCIDENCE OF MYOCARDIAL LESIONS IN POLIOMYELITIS FOUND AT POST-MORTEM EXAMINATION

Author	Total examined	Number showing myocardial changes
Saphir and Wile (1942)	7	6
Peale and Lucchesi (1943)	9	7
Dublin and Larson (1943)	12	2
Saphir (1945)	17	10
Gefter *et al.* (1947)	6	4
Dolgopol and Cragan (1948)	92	16
Ludden and Edwards (1949)	35	14
Spain *et al.* (1950)	16	14

Macroscopic appearance of the heart. Saphir (1945) described the heart as flabby and soft. The muscle was commonly pinkish-grey in colour with a " boiled " appearance. In many specimens there was flattening of the papillary muscles and chordæ tendineæ. The weight of the heart is increased according to Ludden and Edwards (1949) although Spain *et al.* (1950) disagree. Dilatation of the ventricles, especially the right, is described by Gefter *et al.* (1947) and by Ludden and Edwards (1949). Endocardial and epicardial petechiæ are common and may resemble those seen in other acute illnesses complicated by anoxæmia.

Ludden and Edwards (1949) described specimens showing respectively a perforation of the posterior wall of the right atrium and an accompanying hæmopericardium; non-rheumatic verrucous endocarditis of the mitral valve; endarteritis of a patent ductus arteriosus; and obliterative pericarditis. They questioned whether the last two lesions could be attributed to the fatal poliomyelitis, but mitral verrucous endocarditis has been previously described by Luhan (1946).

Microscopic lesions in the myocardium. Later descriptions differ little from those recorded by Saphir and Wile in 1942. Damage to myocardial fibres varies from loss of striation with aggregation of nuclei, cloudiness, and thinning to discrete areas of focal necrosis. Peale and Lucchesi (1943) observed fragmentation of muscle bundles and nuclear pyknosis. Dolgopol and Cragan (1948) described foci in which the fibres have multiple nuclei; they could not say whether the nuclei were derived from the fibres themselves or from blood vessels.

Focal necrotic lesions were first described by Ludden and Edwards (1949). In one specimen there were scattered areas in the posterior wall of the left ventricle in which muscle fibres were replaced by large mononuclear cells in a lacework of connective tissue cells. Although no fibroblastic activity was seen, these areas are described as " healed." Similar areas of " healing " were seen by Baskin *et al.* (1950) and Boucek *et al.* (1949). Spain *et al.* (1950) describe fibroblasts, indicating repair, in two of their specimens, after an illness lasting 22 days.

Damage to the myocardial fibres was usually accompanied by an interstitial exudate consisting of focal collections of lymphocytes and polymorphonuclear cells. Polymorphs predominated in those areas where the muscle fibre damage was greatest. Occasionally the exudate was widespread throughout large areas of myocardium. Collections of cells were found chiefly in the wider bands of connective tissue between muscle fibres, and around the smaller blood vessels. Saphir (1945) and Dolgopol and Cragan (1948) remark that myocardial lesions are frequent where there are sub-epicardial and endocardial petechiæ, the most profuse lesions occurring in the left papillary muscles and ventricular septum. Saphir (1945) found unusual fibrinoid material in the media of the aorta.

Myocarditis is on the whole minor in extent and non-specific in character, similar to the lesions seen in other virus infections such as influenza and mumps. There is a gradation in damage from minimal focal areas of degeneration to patches of necrosis. Polymorphonuclear cells predominate in the earlier and more severe lesions, and later necrotic lesions may show signs of healing.

Electrocardiographic Findings in Poliomyelitis

The earliest electrocardiographic observations to be made in poliomyelitis were those of Peabody *et al.* (1912) who were studying the terminal arrhythmia. An illustration in their paper shows pronounced sinus arrhythmia which was attributed to vagal disturbance.

The first comprehensive report was by Gefter *et al.* (1947). The abnormalities described in this and subsequent papers are summarized in Table II, the most frequently observed changes being in T waves and S–T segments. Gefter *et al.* (1947) found abnormal records more frequently in severe forms of poliomyelitis but this has not been confirmed by others. Frischknecht and Zellweger (1950) suggested that transient T wave changes early in the illness were caused by sympathetic disturbance, whereas those persisting for more than three weeks were due to myocarditis. Among unusual changes they mention the occurrence of auricular systoles on the fifth day of illness. After one year this patient had developed a typical Wolff-Parkinson-White syndrome. The first observations on the Q–T interval in poliomyelitis and its value as an indication of myocardial involvement were made by Joos and Yu (1950).

TABLE II

ELECTROCARDIOGRAPHIC ABNORMALITIES IN POLIOMYELITIS

Author	No. in series	Excessive tachycardia	P wave	P–R interval	QRS complex	S–T segment deviation	T wave
Gefter *et al.* (1947)	226 (32 abnormal)	9	High and peaked in 6	Prolonged in 7	Slurred 1	5	8
Boucek *et al.* (1949)	1	—	—	—	—	Elevation in lead 1	Diphasic
Bradford and Anderson (1950)	155 (20 abnormal)	12	—	2	—	—	16
Firpi *et al.* (1949)	44 (10 abnormal)	—	—	1	—	8	1
Joos and Yu (1950)	23 (7 abnormal)	4	—	1	—	Prolonged Q–Tc in 5	—
Frischknecht and Zellweger (1950)	52 (21 abnormal)	—	Negative in 1	1	W–P–W syndrome in 1	—	18

MATERIAL AND RESULTS

Electrocardiograms were taken in 55 children out of a total of 102 who were admitted to the Children's Hospital, Birmingham, with poliomyelitis during the summer of 1950. Chest leads were taken where indicated but this was technically impossible when patients were in the respirator. In the majority, weekly readings were taken, but in 13 only a single tracing was obtained. Unfortunately no records were obtained in children who later died, as all required immediate treatment in the respirator. It was thus impossible to correlate the electrocardiographic picture and the histological appearance of the heart. Several records were, however, made in 5 other children who required a respirator and survived.

The clinical manifestations were classified as follows: non-paralytic 15; spinal paralytic 28; bulbar 4; bulbospinal 4; encephalitic 2; midbrain syndrome (tremor, ataxia, opsoclonia) 2. The youngest patient was an infant twelve days old whose mother died of fulminating polioencephalitis three days after the infant's birth. The infant had paralysis of all four limbs, but there was no electrocardiographic abnormality.

Abnormal records were obtained from 13 children. No disturbances of rhythm were seen, but 12 children had tachycardia exceeding 150 beats a minute when the first recording was taken. This was not thought to be excessive in view of a fever frequently as high as 103° or 104° F. The results are summarized in Table III.

Q waves. Deep Q waves were present in leads II and III in Case 1 on the 13th day. Q II was no longer present and Q III was smaller on the 158th day (Fig. 1). Persistent deep Q III waves were observed in Case 2, in which there were associated S–T segment changes. In 6 other children Q III was the only abnormality; 2 were 16 months old, 3 were 2 years old, one was 4 years old. Their significance is very doubtful; such waves are common in normal children.

S–T segment and T waves. Cases 3, 4, 5, and 6 showed transient T changes with associated abnormal deviation of S–T segments. The changes occurred in the first three weeks of the illness after which both T waves and S–T segments were normal. In Case 6 the blood pressure was 125/80 on the tenth day, falling to 90/50 on the twentieth day (Fig. 2). In Case 7, who had a most severe attack of poliomyelitis, S–T and T changes persisted for over two months from the onset. It was thought that myocardial damage had been severe (Fig. 3). Cases 8 and 9 had transient

TABLE III

SUMMARY OF ABNORMAL ELECTROCARDIOGRAPHIC FINDINGS IN POLIOMYELITIS

55 PATIENTS EXAMINED: ABNORMAL RECORDS IN 13 CHILDREN

No.	Sex	Age	Clinical Type	Paralysis	Q	S–T	T	P–R	Q–Tc	Notes
1	M	6·4	S.P.	R. lower limb.	+			+		Transient weakness R. ant. tibials
2	M	2·4	S.P.	L. lower limb.	+	+		+		Residual weakness L. ant. tibials
3	F	1·2	S.P.	R. upper and lower limbs and intercostals		+	+		+	Transient paralyses. Complete recovery
4	M	4·9	S.P.	All four limbs and intercostals		+	+			Respirator 3 days. Gross residual weakness all four limbs
5	F	3·9	N.P.	—		+	+			No paralysis
6	F	10·8	B.S.	9 and 10 C.N. R upper limb and both lower limbs		+	+			Recovery bulbar palsy. Residual weakness both lower limbs
7	F	9·3	S.P.	All 4 limbs and intercostals		+	+			Respirator 6 weeks. Gross residual weakness all four limbs
8	F	2·9	B.S.	7, 9, 10. C.N. All four limbs and intercostals			+		+	Respirator 7 weeks. Gross residual weakness all four limbs and intercostals
9	F	13·3	B.S.	7, 9, 10 C.N. R. upper and R. lower limb			+			Recovery bulbar palsies. Weakness R. triceps and ant. tibials
10	M	2·2	S.P.	R. upper limb and intercostals				+	+	Transient intercostal weakness. Residual weakness R. triceps, shoulder girdle
11	F	5·1	B.S.	7. Both upper limbs and intercostals				+	+	Respirator 3 weeks. Residual weakness upper limbs
12	F	6·2	S.P.	Both lower limbs					+	Residual weakness left quadriceps, ant. tibials
13	M	1·5	S.P.	Both lower limbs					+	Residual paralysis both lower limbs

N.P.=non-paralytic S.P.=spinal paralytic B.S.=bulbospinal C.N.=cranial nerves

flattening of T waves early in the illness, returning rapidly to normal. In Case 8, a blood pressure of 134/100 on the tenth day had fallen to 95/70 on the fifty-fifth day.

P–R interval. The P–R interval was prolonged in 4 children, using the standards for age and heart rate recommended by Ashman and Hull (1941). In two, there was also prolongation of the Q–Tc interval.

Q–T interval. Following the method of Abrahams (1949), the Q–T interval was measured in each record taken. Corrected values were calculated according to Bazett's formula (1920). Taran and Szilagyi (1947) take 0·405 seconds as the upper limit of normal for the corrected Q–T interval or Q–Tc in childhood. Abrahams (1949) recommends a higher value of 0·422 seconds, which has been adopted as the upper limit of normality in this series. The duration of electrical systole as measured by Q–Tc was prolonged in 6 patients.

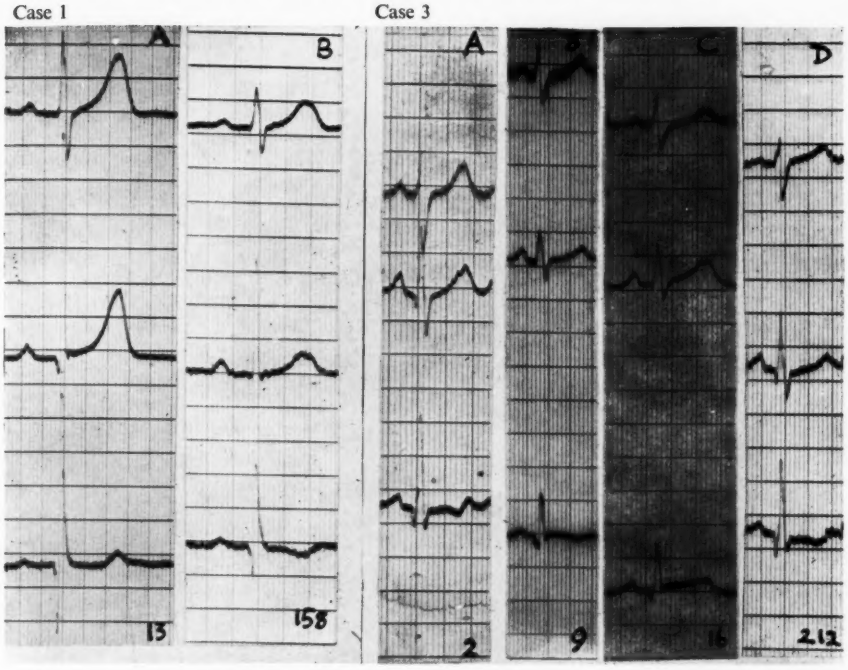

FIG. 1.—Case 1. (A) 13th day, Q2 and deep Q3; P–R, 0·18 sec. (B) 158th day, Q3 smaller; P–R, 0·16 sec. Case 3. (A) 2nd day, depression, S–T3; Biphasic T3; Q–Tc, 0·416 sec. (B) 9th day, S–T3 normal; T3 inverted; Q–Tc, 0·454 sec. (C) 16th day, S–T3 normal; T3 upright; Q–Tc, 0·432 sec. (D) 212th day, depression S–T3; Q–Tc, 0·462 sec.

Case 3. Q–Tc was within normal limits (0·416 sec.) on the second day of illness. It rose on the ninth day to 0·454 sec. and was 0·432 on the sixteenth day. A final reading on 212th day was 0·462 sec. An apical systolic murmur was audible at the time Q–Tc was first known to be prolonged (Fig. 1).

Case 8. There was flattening of T waves early in the illness. On the 71st day Q–Tc was 0·432 sec. (Fig. 5).

Case 10. On the ninth day of illness P–R, 0·13 sec.; Q–Tc, 0·377 sec. By the 33rd day, P–R, 0·16 sec.; Q–Tc, 0·430 sec. Intercostal weakness present from 8th to 29th day. On 228th day, P–R, 0·13 sec.; Q–Tc, 0·345 sec.

Case 11. On the 21st day of illness, P–R, 0·16 sec.; Q–Tc, 0·444 sec.; By 42nd day, P–R, 0·17 sec.; Q–Tc, 0·453 sec. Intercostal weakness present from 4th to 21st day (Fig. 4).

Case 12. Q–Tc was 0·449 sec. on fourteenth day. Further readings of Q–Tc were 0·466 sec. and 0·449 sec. on 35th and 108th days. No respiratory weakness (Fig. 4).

Case 13. Q–Tc was 0·435 sec. on the twelfth day. No respiratory weakness.

In 4 patients there was respiratory muscle weakness. In Cases 3, 8, and 10, Q–Tc was normal at the onset of respiratory weakness. The duration of respiratory weakness before Q–Tc was prolonged was 7 days in Case 3, 65 days in Case 8, and 25 days in Case 10. In Case 10, Q–Tc had returned to normal on 228th day of illness. In Case 11, the data are incomplete, but prolongation was present 17 days after the onset of respiratory weakness and remained so 21 days later.

DISCUSSION

The preponderance of histological cardiac lesions in children is perhaps simply a reflection of the higher incidence of the disease itself in younger subjects. The youngest on record is that of

Baskin *et al.* (1950) who found severe lesions in a five-day-old infant. Ludden and Edwards (1949), whose series included many adults, thought that the cardiac damage was most severe in older patients, although this was not confirmed by Spain *et al.* (1950). Ludden and Edwards found that

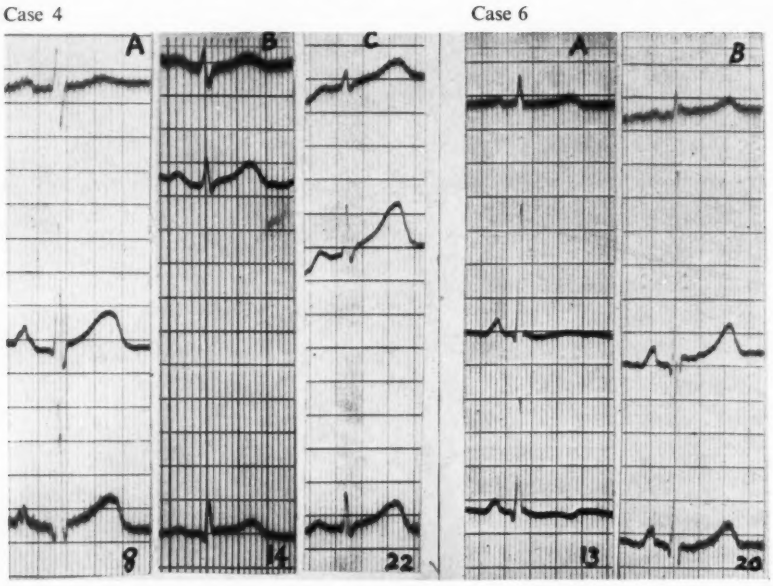

FIG. 2.—Case 4. (A) 8th day, elevation S–T2 and 3; T2 and T3 domed. (B) 14th day, elevation of S–T2 and 3. (C) 22nd day, T3 increased in amplitude. Case 6. (A) 13th day, depression of ST–2 and 3; flat T waves. (B) 20th day, S–T2 and 3 normal; T waves normal.

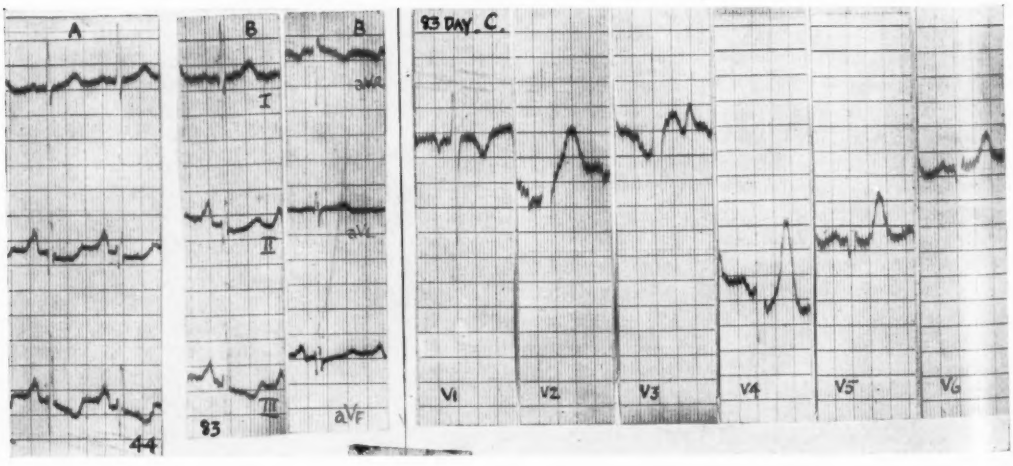

FIG. 3.—Case 7. (A) 44th day, depression S–T2 and 3; inverted T2 and 3. (B) 83rd day, T2 normal; T3 inverted. (C) 83rd day, S–T elevated in V2 and 3; bifid T in V3; tall T in V4.

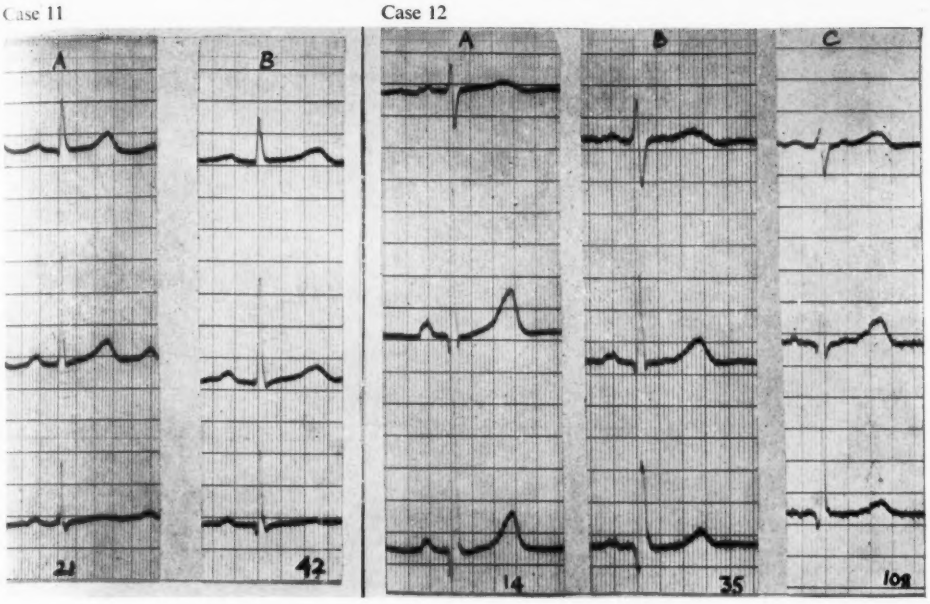

FIG. 4.—Case 11. (A) 21st day, P–R, 0·16 sec.; Q–Tc, 0·444 sec. (B) 42nd day, P–R, 0·18 sec.; Q–Tc, 0·453 sec. Case 12. (A) 14th day, P–R, 0·14 sec.; Q–Tc, 0·449 sec. (B) 35th day, P–R, 0·14 sec.; Q–Tc, 0·466 sec. (C) 108th day, P–R, 0·13 sec.; Q–Tc, 0·449 sec.

males were more often affected than females, but this too is probably a reflection of the long-recognized higher incidence of poliomyelitis in males. In the majority death took place early in the disease in those showing cardiac damage. 12 of 16 cases reported by Dolgopol and Cragan (1948) died in the first five days of the illness. Thirteen of Ludden and Edward's series (1949) died in less than 11 days from the onset.

In no series has it been possible to correlate the clinical type of disease with the presence of histological myocarditis, which may apparently follow any severe form. Saphir and Wile (1942) suspected myocarditis if the patient became suddenly worse, or if he had either tachycardia or bradycardia together with cyanosis. On the other hand Ludden and Edwards (1949) recognized that tachycardia, irregularity of the pulse, dyspnoea, and cyanosis are common terminal findings in poliomyelitis, whether or not myocarditis is present. In three of their patients a basal systolic murmur was audible, and one of them later proved to have a moderately severe myocarditis. It is difficult to say whether myocarditis is responsible for sudden death in poliomyelitis. Sudden death took place in six of Ludden and Edward's series, three of whom had myocarditis, but in these bulbar damage was severe and might have been responsible.

Pathogenesis of Myocarditis in Poliomyelitis. Before considering the possible role played by the poliomyelitis virus, other alternative ætiological factors have to be mentioned. Myocarditis is a well-recognized histological feature in fatal bronchopneumonia (Stone, 1922). Bronchopneumonia is a frequent post-mortem finding in poliomyelitis and by some has been held responsible for myocardial changes. Myocarditis may, however, occur in the absence of pneumonia, and pneumonia without myocardial changes (Saphir and Wile, 1942). Six of Dolgopol and Cragan's patients (1948) died so early that bacterial invasion of the lungs was probably too slight to cause cardiac damage. An opposing view is taken by Bell (1949) who, quoting the work of Clawson considers that respiratory infection is the probable cause of myocarditis.

French and Weller (1942) showed that sulphonamide drugs may cause myocardial damage in both the experimental animal and in man, but myocardial changes in poliomyelitis were recognized before the

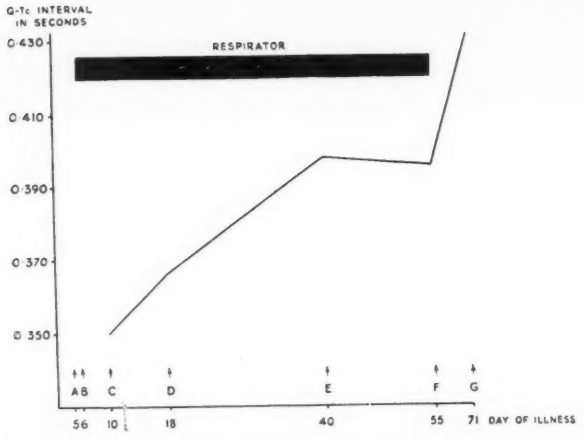

FIG. 5.—Case 8. Showing increasing length of Q–Tc interval related to respiratory muscle paralysis. (A) Day 5, onset of bulbar palsy. (B) Day 6, intercostal weakness. (C) Day 10, T II and III flat. (D) Day 18, T II and III flat. (E) Day 40, T II and III flat. (F) Day 55, improvement in intercostal weakness. (G) Day 71, normal T II and III. Prolonged Q–Tc.

introduction of therapeutic sulphonamides. It is consequently unlikely that these drugs play any part in producing lesions in poliomyelitis.

The patient described by Clark (1938) had been given horse serum as a therapeutic measure early in the disease. Signs of serum sensitivity appeared before death. Diffuse interstitial myocarditis was revealed at necropsy, and was attributed to some form of hypersensitivity reaction. Although sera have been abandoned in the treatment of poliomyelitis, they have to be considered as possibly responsible for myocardial damage. Saphir (1945) whose 10 patients with myocarditis had been given serum does not believe that it was responsible for the cardiac lesion. Similarly, Dolgopol and Cragan (1948) and Ludden and Edwards (1949) conclude that horse serum could not be responsible for a hypersensitivity reaction causing myocarditis when it had been given for so short a time.

Poliomyelitis virus was isolated for the first time from the heart of a fatal case in 1949 (quoted by Jungeblut, 1950). The pathway by which poliomyelitis virus reaches the heart is not known. The evidence that virus may be present in the blood is scanty. Ward *et al.* (1946), isolated virus from the blood of only one out of 111 patients with poliomyelitis, but the possibility of a viræmic phase is suggested by the presence of inflammatory lesions in the pectoral muscles and diaphragm (Hassin, 1943), and the isolation of poliomyelitis virus from paralysed muscle in the acute stage of the illness (Jungeblut and Stevens, 1950).

Pearce (1950) has reviewed the mechanisms involved in the production of virus myocarditis in the experimental animal. He showed that in the rabbit myocarditis could be induced with several different viruses, not previously thought to have any cardiotropic activity, provided there was anoxæmia of the cardiac muscle. The results of such experiments must be applied to man with reservation, but it may be that a similar mechanism is involved in the pathogenesis of the human disease.

The relationship of electrocardiographic changes to histological damage is still imperfectly understood. Among the few reported cases is that of Boucek *et al.* (1949) in which S–T and T changes were associated with concentrated damage in the left ventricle. Bradford and Anderson (1950) found abnormal records in 4 of 5 fatal cases, 3 of whom had myocarditis. Frischknecht and Zellweger (1950) found no histological abnormality in the heart in 2 patients who had shown abnormal T waves on the fifth day of illness.

Present Series. The pattern of electrocardiographic abnormalities corresponds to those reported in previous series. Abnormal records were obtained in 13 of 55 children examined, the most frequently occurring abnormalities being in the S–T segments and T waves. The occurrence of

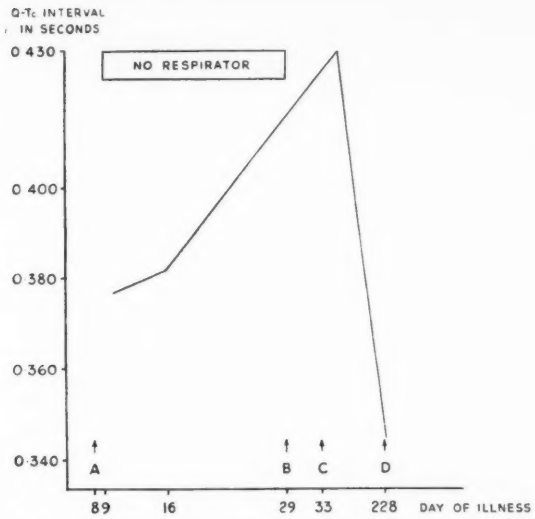

FIG. 6.—Case 10. Showing increase in Q–Tc interval related to respiratory muscle paralysis. Q–Tc returned to normal on 228th day of illness. (A) Day 8, onset of intercostal weakness. (B) Day 29, recovery from intercostal weakness. (C) Day 33, prolonged Q–Tc. (D) Day 228, normal Q–Tc.

respiratory muscle paralysis in 4 of 6 children in whom there was prolongation of the Q–Tc interval has been mentioned previously. Cardiographic abnormalities occurred more often in those with respiratory muscle paralysis than in those not so affected. Of 7 with respiratory paralysis, 6 had abnormal cardiograms, while of 48 without respiratory paralysis, only 7 showed abnormal records. These results may be compared with those of Joos and Yu (1950), in which three children had intercostal weakness, the Q–Tc interval being prolonged in two; in 20 without respiratory paralysis Q–Tc was prolonged in three.

The incidence of electrocardiographic abnormalities in the different clinical groups of poliomyelitis shows the highest incidence to be in the bulbospinal group, the lowest in the non-paralytic. All four bulbospinal patients had abnormal records. Eight of 25 records in spinal paralytic cases were abnormal. Only one of 15 non-paralytic cases was abnormal. No abnormal records were obtained in the bulbar or encephalitic patients examined, nor in two with an unusual midbrain syndrome. The age of the patient did not appear to be related to the abnormalities in the cardiogram. Prolongation of the Q–Tc interval was not, however, seen in any child over six years of age.

The clinical evidence of myocardial disease was small. Tachycardia with cyanosis and dyspnœa are usual findings in respiratory paralysis and could not be attributed with any confidence to cardiac disease. In no case was there enlargement of the heart. In one there was a transient apical systolic murmur at a time when the Q–Tc interval was prolonged (Case 3). This may have indicated true myocardial involvement. There was temporary elevation of the blood pressure in Cases 6 and 8, both of whom had bulbospinal involvement. The association of cardiographic changes with respiratory muscle paralysis suggests that in some they may be related to anoxæmia. The effect of oxygenation on the electrocardiogram of patients in the respirator may give a more satisfactory answer to this question.

Summary

Electrocardiograms were taken in 55 children with poliomyelitis. Abnormalities were found in 13. They were non-specific in character and included Q wave abnormalities in 2, S–T segment and T wave changes in 5, T wave changes in 2, prolongation of P–R interval in 4, and prolongation of Q–Tc in 6.

The lowest incidence of changes was in the non-paralytic group, the highest in the bulbospinal. The relationship of electrocardiographic changes to respiratory muscle paralysis is discussed.

My thanks are due to the Physicians to the Children's Hospital, Birmingham, for permission to investigate their patients. In particular I have to thank Dr. Clifford Parsons and Professor J. M. Smellie for their advice during the preparation of this paper, and Miss J. Wright who took several of the recordings.

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COMPARISON OF DIFFERENT SYSTEMS OF VECTORCARDIOGRAPHY

BY

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It is usual for various investigators to use their own system of vectorcardiography. Such a system is characterized by the place of the electrodes and the way in which the vectorcardiogram is deduced from the potential differences obtained.

At present the system according to Duchosal and Sulzer (1949) and the one proposed by Wilson *et al.* (1947) are much in use. The equilateral tetrahedron proposed by the latter is a generalization of the equilateral triangle of Einthoven *et al.* (1913). In addition the present authors have proposed and used another fundamentally different method, based on the following line of thought. By this method, the principle of which is physically well founded (1946), the vectorcardiogram may be deduced from three potential differences. That is to say, if the electromotive force of the heart may be considered as that of a single dipole, there will be a linear relation between each potential difference V_p-V_q and the three orthogonal components X, Y, Z of the heart vector:

$$V_p-V_q=aX+bY+cZ$$

The coefficients a, b, c have been determined with the aid of a model, but this can also be done in another way, e.g. by cadaver experiments. From three similar equations, the three unknowns X, Y, Z can be expressed in three potential differences.

These different systems have but rarely been compared with each other: Duchosal and Sulzer compared theirs, so far as it is applied to the frontal projection, with the system of Einthoven; Milnor *et al.* (1951) did so in a similar way, as regards Duchosal's and Sulzer's system and those of Wilson *et al.*, and the one according to Milovanovich used in France (1948).

Lately Grishman *et al.* (1951) have recorded vectorcardiograms in three ways, namely with the aid of the regular tetrahedron, according to Duchosal and Sulzer, and the one according to Arrighi.

In this paper we shall report the results of a comparative investigation of three systems, namely the two we have proposed and used, and that of the equilateral tetrahedron.

The two Systems used by Us

In principle each set of four electrode positions can be used, but, in order to deduce the components of the heart vector from them, one has to use the coefficients corresponding with it (Burger and van Milaan, 1947). A choice of two sets, called here B_1 and R_2, has been made out of an infinite number of possibilities.

B_1. The electrodes were connected to the left arm (L), right arm (R), and left leg (F), while a fourth was placed on the sternum at the level of the axilla (B). The potential differences have been measured with respect to the right arm (R), taken as zero (Fig. 1). The component X is the lateral, positive to the left. The component Y is the sagittal, positive to the front. The component Z is

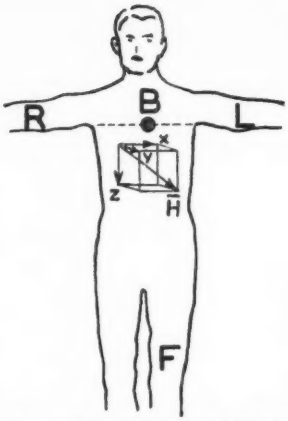

FIG. 1.—Positions of the electrodes in the system B_1. R=right arm, L=left arm, F=left leg, B=electrode on the sternum.

the longitudinal, positive footward. The potential differences are indicated by the following abbreviation:

$$V_L - V_R = LR$$

The components X, Y, Z of the heart vector have been composed out of the three potential differences LR, BR, and FR in the following way:

$$X = 54LR + 8BR + 16FR$$
$$Y = -12LR + 40BR + 26FR$$
$$Z = -10LR - 6BR + 26FR$$

These equations give relative values. The heart vector is obtained in absolute measure (volt. cm.²) if X, Y, Z is multiplied by about 25 according to these equations. The potential differences are expressed in volts.

R_2. Again an electrode is connected to the left leg (F). The other three (S, R_b, L_b) are at the level of the axilla. S has been placed centrally on the vertebral column (Fig. 2). R_b and L_b are symmetrical at a distance of 50 per cent of the thorax breadth at the level of the axilla. In practice this means that the circular electrodes, 4 cm. in diameter, touch the midclavicular line at the medial side.

The components of the heart vector have now been composed out of three potential differences, L_bR_b, SR_b, FR_b, according to the equations:

$$X = 34L_bR_b + 20SR_b + 20FR_b$$
$$Y = 4L_bR_b - 36SR_b + 8FR_b$$
$$Z = -8L_bR_b - 16SR_b + 22FR_b$$

As is seen in Fig. 2 the electrodes are situated at the level of the axilla alternatively between two electrodes of the system B_1, so that in this respect the two systems differ considerably. The R_2 system has been chosen from many other possibilities because it has a mathematical advantage. In this case one is far from the undesirable situation that the four electrode places lie in one plane in the image space (Burger and van Milaan, 1948). If this had been so, then the fourth potential difference could be deduced from the three and would be no independent datum. The coefficients from the equation (B_1) and (R_2) have been deduced from measurements on a model of the human body in a way, previously described (Burger and van Milaan, 1947).

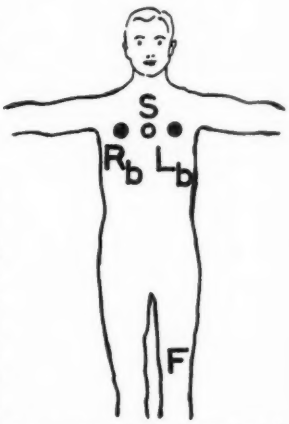

FIG. 2.—Positions of the electrodes in the system R_2. Rb and Lb= electrodes on the chest, F=left leg, S=electrode on the back.

THE SYSTEM OF THE EQUILATERAL TETRAHEDRON (W_4)

In this system three electrodes are connected to the arms and the left leg (R, L, F) while the fourth (W) is placed on the back at the level of the seventh thoracic vertebra and 2 cm. to the left of the vertebral column (Fig. 3). The relation of the heart vector and potential difference is presented by the authors (Wilson *et al.*, 1947) in geometrical terms. According to their opinion the four electrodes in the spatial diagram are located at the apices of an equilateral tetrahedron, of which the frontal place RLF is an equilateral triangle (as with Einthoven c.s.) in a perpendicular plane. This geometrical relation can also be expressed algebraically such that the components of the

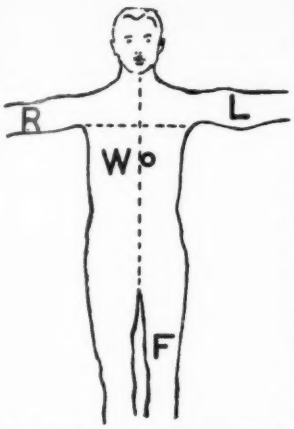

FIG. 3.—Postition of the electrodes in the system W_4. R=right arm, L=left arm, W=electrode on the back.

heart vector appear as linear functions of three potential differences. From an elementary computation it follows, that:

$$X = 40LR$$
$$Y = -23LR + 46FR$$
$$Z = 16LR - 49WR + 16FR$$

In contrast to the two previous cases (B_1 and R_2) here the numerical coefficients are only determined as far as their ratio is concerned; they may be multiplied by any given factor. This factor has been chosen such that the correspondence with B_1 and R_2 is as nearly good as possible. This flatters, therefore, the correspondence between W_4 and the two other systems. On the other hand the relation of the scales of the other two systems has been determined by the measurement in the model, and the agreement or disagreement of the sizes of the vectorcardiogram of B_1 and R_2 is therefore a criterion of the correctness of our principal starting point, which does not hold for W_4.

MEASUREMENTS

The vectorcardiograms have been made by the universal vectorcardiograph, previously described (Becking *et. al.*, 1950). With the aid of the knobs on the frontplate, the coefficients B_1, R_2 W_4 had been adjusted successively. Of each vectorcardiogram the frontal and horizontal aspect is photographed. So there are six loops for the three compared systems. This has been performed for 115 normal and pathological subjects.

COMPARISON OF THE THREE SYSTEMS

To obtain a quantitative measure for the correspondence of the vectorcardiogram according to the different systems, the quality of this correspondence has been indicated by a mark. The mark 10 gives then an ideal correspondence, as is found with successive heart beats, measured by the same system, while 0 means that the two curves have not a single point of correspondence. These extreme cases were not encountered. 5 gives the border between sufficient and insufficient. Naturally, such an estimation is subjective but it can be used as a measure of correspondence. Independently of each other the authors have obtained marks in this way, after which a final opinion was drawn up. A few months later many of the marks were again determined, in which case there was rarely a difference of more than one unit. The significance of the marks is illustrated by Fig. 4, in which very good, very bad, and sufficient correspondence are shown. In estimating these marks a number of criteria played a part such as size, direction of the largest diameter, sense of rotation relation of right and left part, and details like notches.

For every subject the correspondence of the vectorcardiogram according to B_1, R_2 and W_4 was indicated by three marks for the frontal projection and three for the horizontal one. In order to be able to draw conclusions from the $6 \times 115 = 690$ cases the averages were computed for 115 marks, representing the quality of correspondence respectively of the frontal, and of the horizontal projection of each set of two systems. Moreover, for each of these six averages the standard error has been computed.

Fig. 5 shows the result of these calculations. The standard error arose owing to superposition of the uncertainty in the estimation of each case and the difference between various subjects. As is seen the differences between the average marks for the three combinations B_1R_2, W_4B_1, and W_4R_2, are a few times larger than the error in each of these averages. So these differences may be considered to be significant. Fig. 5 shows that, for the frontal projection as well as for the horizontal one, the correspondence of B_1 and R_2 is the best, while W_4R_2 shows the worst result.

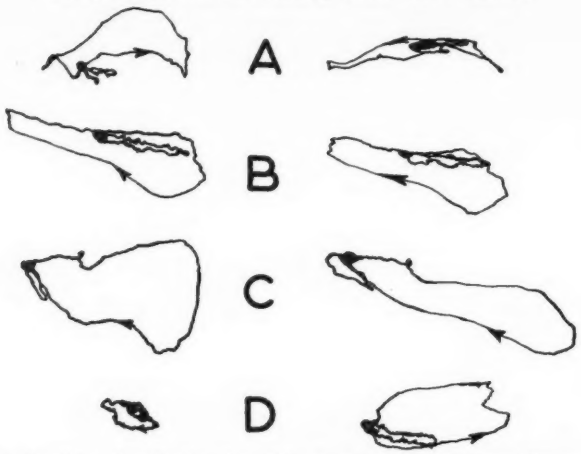

FIG. 4.—Examples of estimation of the correspondence between different systems. (A) frontal projection, W_4 left, R_2 right, bad correspondence; mark 3 (ratio of the deflections right and left is considerably different). (B) frontal projection, B_1 left, R_2 right, very good correspondence; mark 9. (C) frontal projection, W_4 left, B_1 right, sufficient correspondence; mark 6. (D) horizontal projection, W_4 left, R_2 right, bad correspondence; mark 2.

The rather favourable result of the comparison W_4B_1 frontal must be attributed to the fact that the frontal projection of W_4 and B_1 is mainly composed of the same potential differences, be it with other coefficients. There is therefore approximately a mathematical relation (linear transformation) between these curves. All kinds of details (e.g. notches) occur with both. As a result of this relation the standard error of the marks for W_4B_1 frontal is small (0, 07).

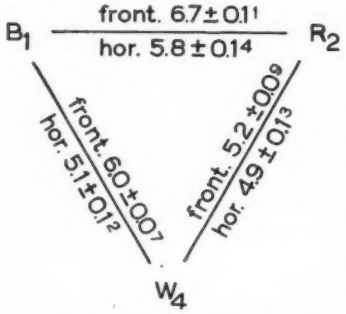

FIG. 5.—Averages of the estimations of all compared cases. Front. 6·7±0·1 indicates that the correspondence of the frontal projections of the vectorcardiograms according to system B_1 and R_2 is expressed by the average mark 6·7 and that the standard error in it amounts to 0·1.

The quality for the horizontal projection is less satisfactory than for the vertical ones. This is a result of the uncertainty in the sagittal component of the heart vector in each of these methods. This again is connected with the small sagittal dimension of the thorax, which is not so very much larger than the corresponding dimension of the heart. The large longitudinal dimension of the thorax, on the other hand, enables us to say with a fair degree of certainty, something about the vertical component of the heart vector.

If a choice has to be made between the three systems B_1, R_2 and W_4, and this choice has to be based on the quality of their correspondence, then B_1 and R_2 are to be preferred to W_4. These first two systems are also preferable because of their being rationally founded. Generally they give in practice a satisfactory correspondence. Furthermore, W_4 has the practical drawback that the sagittal component is often so small that the horizontal projection shows no details. But, on the other hand, W_4 has unquestionably advantages, namely the use of extremity leads, and the position of the back electrode, which is located farther from the heart than the chest electrodes in our systems B_1 and R_2. By means of a suitable selection of the coefficients, while maintaining the places of the electrodes, a rationally founded W_4 could be obtained which would contain the advantages mentioned.

In general, however, the three systems so far used by us do mostly give pathological particulars

in an analogous way. By all three systems, these particulars are most strikingly visualized with left bundle branch block.

The Cause of Unsatisfactory Correspondence

A. If the electrical action of the heart can really be described by a single dipole, there must be a simple mathematical relation between the vectorcardiograms of one patient, recorded according to different systems. It must be possible to transform one curve into another by a so-called linear transformation. By this we understand a mathematical transformation of a figure, e.g. by rotation or enlargement. When rotation and enlargement, etc., are small, the correspondence is considered to be good. If that is not the case the reason of such a bad correspondence has to be looked for in the tissues surrounding the heart, which define the electrical properties of the thorax. By making another choice of the coefficients previously mentioned, the correspondence could be improved. However, this holds good only for the investigated subject. The differences between the individuals are so great, however, that it will not be possible to come to a satisfactory correspondence for all cases, when using one and the same set of coefficients. On the other hand, we are not in a position to determine the coefficients for each individual.

B. Another possibility is that a bad correspondence between two systems is a result of the fact that the electrical action of the heart cannot be thought of as being the effect of one single dipole. In fact in the heart will always be a spatially distributed dipole action, and as the heart is not so very small in respect to the thorax, the dipole in one part of the heart will give another potential distribution than an equal dipole in another part of it. The dipoles may then not simply be added. This condition might be specially important when one of the electrodes is placed close to the heart. In a case like that, it would be possible, for instance, for one system to show a local peculiarity in the vectorcardiogram, which is not to be found in the other system, not even in a deformed position.

That the large dimensions of the heart can be of importance, is seen with extrasystoles. The electrical action of the heart is here different from that in a normal heart contraction, but the surroundings of the heart, which define the connection between heart vector and lead, are the same. Yet it is sometimes seen that the correspondence of the vectorcardiogram in different systems is better with the normal beat than with an extrasystole or the reverse. This can only be a result of the different position in the heart where the excitation originates, and the different spatial distribution of it during the systole and diastole.

Summary

Three systems of vectorcardiography, using different positions of the electrodes, are compared. The correspondence of two systems of the authors is sufficient; that of these two with the system of the equilateral tetrahedron is less satisfactory. Possible causes of bad correspondence in some cases are discussed.

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THE SMALL PULMONARY VESSELS IN MITRAL STENOSIS

BY

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The association of pulmonary arteriosclerosis with mitral stenosis has long been recognized: Posselt (1909) reviewing all the cases of pulmonary arteriosclerosis published in the 19th century found that mitral stenosis was present in 40 per cent of them. In early accounts, however, attention was directed only to atheroma of the main pulmonary arterial branches, and later descriptions of changes in the small intrapulmonary vessels are difficult to interpret because of differences in terminology. Brenner (1935) gave an excellent account of the morphology of the pulmonary vasculature and his definitions have been adhered to in this paper.

In view of the increasing number of cases of mitral stenosis treated by valvulotomy it is important to define exactly the changes occurring in the small pulmonary vessels to decide whether such changes are likely to continue obstructing the blood flow after operation. The small pulmonary arteries, arterioles, venules, and small veins have been examined in the present investigation, since thickening of the wall of these vessels is likely to bring about significant narrowing of the total vascular lumen.

Material and methods. Sections of the lung from 105 cases of mitral stenosis coming to autopsy in this department in the last 14 years were examined microscopically. As far as possible sections from two separate blocks were prepared in each case and stained by Hart's method for elastic tissue and van Gieson's connective tissue stain. Selected sections were stained with Masson's trichrome stain. Sections were examined in random order and without reference to other details of the case. Changes observed in small arteries, arterioles, venules, and small veins were recorded. The part of the lung from which the original blocks had been taken was unknown. Details of each case were obtained from autopsy records. Right ventricular hypertrophy was considered to be present when a thickness of 5 mm. or more had been recorded. The degree of mitral stenosis was divided into four groups (1) slight or doubtful, admitting two fingers with difficulty, (2) moderate, admitting one finger, (3) severe, admitting one fingertip, and (4) gross, not admitting the tip of the little finger.

In addition, 70 control cases were selected from routine autopsy records, 10 from each of second to eighth decades (inclusive), and divided in the proportion of 4 men to 6 women (the approximate relationship between the sexes in the mitral stenosis series). Chronic pulmonary and cardiovascular-renal disease were excluded from the control series as being possibly associated with some degree of pulmonary hypertension. Sections from the lungs of these cases were examined in the manner previously detailed. Three cases were excluded following microscopic examination since conditions that might be associated with pulmonary hypertension were present although not adequately emphasized in the records.

RESULTS

Of the 105 cases of mitral stenosis examined 42 were men and 63 women. The age at death ranged from 15–79 years. (Decades: II–6; III–15; IV–22; V–32; VI–15; VII–9; VIII–6). All cases over 50 showed something more than the narrowing of the mitral orifice, e.g. adherence of valve cusps, calcification, or vascularization of leaflets.

The degree of mitral stenosis was slight or doubtful in 9 cases, moderate in 48, severe in 33, and gross in 10 cases. In 5 the degree of mitral stenosis had not been recorded at autopsy. Right ventricular hypertrophy was present in 56 cases, absent in 25, and had not been recorded in 24 cases.

Arterioles and Venules. Normal pulmonary arterioles (Brenner, 1935) are indistinguishable from pulmonary venules, both being below 0·1 mm. in external diameter and consisting of a single elastic lamina enclosing an endothelial tube (Fig. 1). Occasional muscle cells are present in interstices in the elastic layer. In some cases of mitral stenosis vessels of these dimensions were seen to have a more or less well-defined media bounded externally by a thick elastic lamina like that forming the wall of the normal arteriole and internally in most cases by a more faintly staining subendothelial elastic fibril (Fig. 2). The appearance was not so regular as that of the small muscular arteries where the external and internal elastic laminæ were of about equal thickness and depth of staining (Fig. 4). In longitudinal section the thickness of the wall varied abruptly along the course of the vessel. The media consisted of circularly directed muscle fibres with occasional strands of collagen and branching fibrils of elastic tissue.

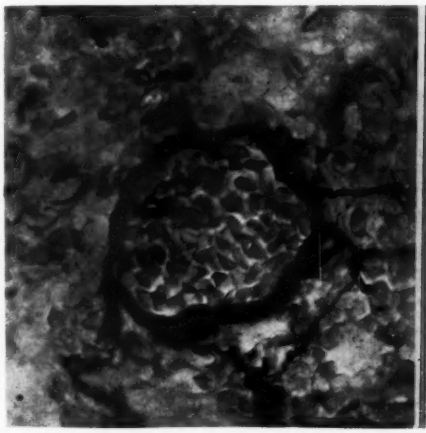

FIG. 1.—Normal pulmonary arteriole. The wall consists of a single elastic lamina. ×700: Hart-van Gieson.

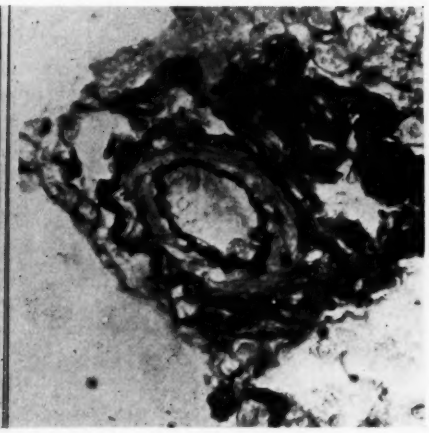

FIG. 2.—Muscularized arteriole in a case of mitral stenosis. A well defined muscular media and internal elastica can be seen. ×700: Hart-van Gieson.

Other vessels of this size showed thickening of the wall due to fibrous tissue intervening between the elastic lamina and the endothelium (Fig. 3). In every section examined some arterioles and venules retained their normal structure. In many cases varying proportions of both the above changes were seen. Examination of the control cases failed to reveal any muscularization of the arterioles, but fibrous intimal thickening, of as great severity in some instances, was observed.

Table I gives the proportion of cases showing arteriolar or venular change in each series and relates these to the age at death (in two groups of 11–40 and 41–80 years). The type of change is recorded only when it was diffuse and readily identifiable. Cases showing both types of change are recorded as of " mixed " morphology. 40 per cent of mitral stenosis cases showed muscularization of pulmonary arterioles which was more frequent (63%) in those dying under 41 years of age than in those dying after this (24%). About half the cases in each age group showed diffuse fibrous change (54% and 53% respectively) as compared with only 17 per cent in the younger control group. In the older control group this type of change was found in 47 per cent.

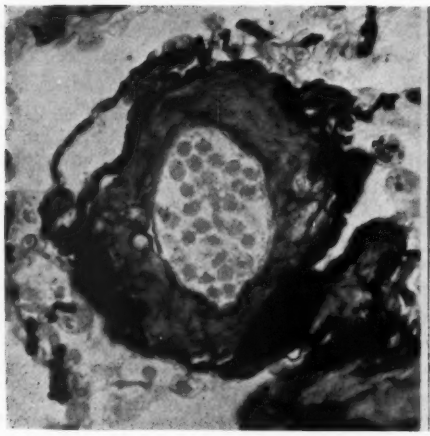

FIG. 3.—Gross fibrous intimal thickening of an arteriole or venule in a case of mitral stenosis. ×550: Hart-van Gieson.

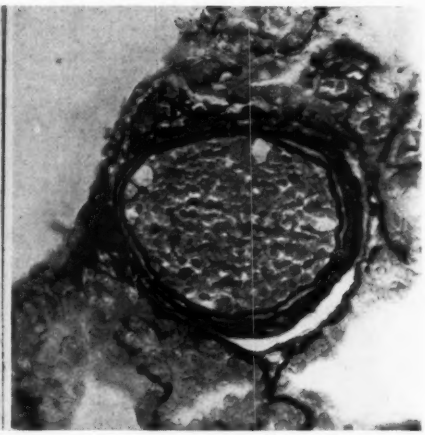

FIG. 4.—Normal small pulmonary artery. The media is thin and bounded by well defined external and internal elastic laminæ. ×350: Hart-van Gieson.

TABLE I

CHANGES IN PULMONARY ARTERIOLES AND VENULES RELATED TO AGE AT DEATH

	No change or slight inconstant change	Diffuse change		
		Muscularization	Mixed	Fibrous
Controls below 40 years	24 (83%)	0	0	5 (17%)
Controls 41 years and over	20 (53%)	0	0	18 (47%)
Mitral stenosis below 40 years ..	11 (26%)	9 (21%)	18 (42%)	5 (12%)
Mitral stenosis 41 years and over ..	25 (40%)	4 (6%)	11 (18%)	22 (35%)

Figures in brackets show the percentage of the total number of cases in each group (approx.)

Table II relates the number of cases showing each type of change to the degree of mitral stenosis. In those with slight or doubtful stenosis no muscularization of arterioles was noted, but 27 per cent of those with moderate, 58 per cent of those with severe, and 80 per cent of those with gross stenosis showed muscular change.

Small Arteries. Small muscular arteries (Brenner, 1935) are vessels of 0·1–1 mm. external diameter with a media occupying 6–32 per cent of this measurement and consisting mainly of circularly directed smooth muscle cells with an occasional elastic fibril (Fig. 4). The media is bounded by well defined internal and external elastic laminae and the endothelial lining rests directly on the former.

Intimal thickening was commonly seen both in the mitral stenosis and in the control series and consisted usually in a segmental or circumferential splitting of the elastica interna to form one or more additional laminæ or layers of fibrils internal to it. A varying number of longitudinally directed muscle cells were present in the interstices. Fibrous tissue tended to replace this musculo-elastic structure especially in cases dying in the later decades.

TABLE II

CHANGES IN PULMONARY ARTERIOLES AND VENULES RELATED TO SEVERITY OF MITRAL STENOSIS

Degree of Mitral Stenosis	Muscularization	Mixed	Fibrous	Total number of cases *
Slight or doubtful	0	0	5	9
Moderate	5	8	14	48
Severe	5	14	6	33
Gross	2	6	0	10

* In the remaining 5 cases, the degree of stenosis was not recorded (one showed muscularization, one mixed change, one fibrosis, and two an insignificant degree of change).

Changes in the media and especially muscular hypertrophy were difficult to interpret. It is uncertain whether all muscular arteries examined showed the same degree of terminal constriction or dilatation. Thus in some there was much crenation of elastic layers, suggesting that the lumen might be artificially reduced and the thickness of the wall increased. It was difficult at times to distinguish between hypertrophied small pulmonary arteries and bronchial arteries with condensation of elastic tissue around the periphery of the media simulating an external elastic lamina. However, in most cases with much muscularization of arterioles, medial hypertrophy of the small arteries was present (Fig. 5); points of narrowing of the media were seen in some of these hypertrophied vessels. Medial and intimal changes in the small arteries varied from vessel to vessel in the same section. Changes recorded in Table III represent at least reduplication of the elastica interna in the majority of vessels.

Intimal thickening in the controls exactly resembled that in the mitral stenosis series, but medial hypertrophy was not seen. Diffuse intimal thickening of the small muscular arteries occurred in 73 per cent of cases of mitral stenosis and in 59 per cent of the controls.

TABLE III

CHANGES IN SMALL MUSCULAR ARTERIES AND VEINS RELATED TO AGE AT DEATH

	Small arteries		Small veins	
	Controls	Mitral stenosis	Controls	Mitral stenosis
Below 40 years	13 (45%)	23 (53·5%)	4 (14%)	30 (70%)
41 years and over	27 (71%)	54 (87%)	29 (76%)	55 (89%)

Figures in brackets show percentage of total number of cases in each group (approx.)

Small Veins. Small pulmonary veins maintain the simple structure of the venule up to a diameter of about 0·2 mm. The structure of the wall is always more irregular than that of the small arteries consisting of elastic fibres interspersed with connective tissue and a few muscle cells. The wall of vessels up to 1 mm. in diameter only occupies 2–7 per cent of the external diameter and there is no well defined elastica externa, the media and adventitia tending to blend (Brenner, 1935).

Fibrous intimal thickening of small veins with a variable admixture of fibrillary elastic tissues was found to be a striking feature of cases of mitral stenosis (Fig. 6). Muscle cells were not prominent. In the control series similar changes were seen often to the same extent. Diffuse, well-marked thickening was present in 81 per cent of cases of mitral stenosis examined and in 49 per cent of controls (Table III). The difference was greater in the younger group (70% in cases under 40 with mitral stenosis compared with 14% of controls).

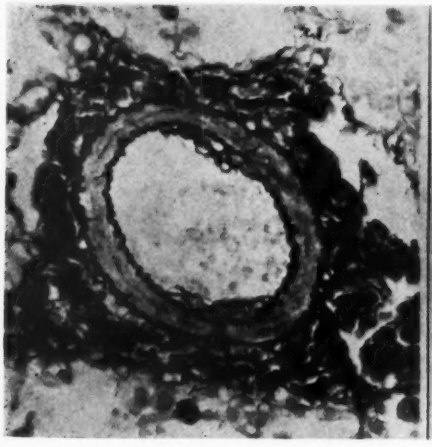

FIG. 5.—Hypertrophy of the media of a small pulmonary artery in a case of mitral stenosis. Localized narrowing of the media is present at one point in its circumference and there is a little segmental musculo elastic intimal thickening. The adventitia is thickened. ×350: Hart-van Gieson.

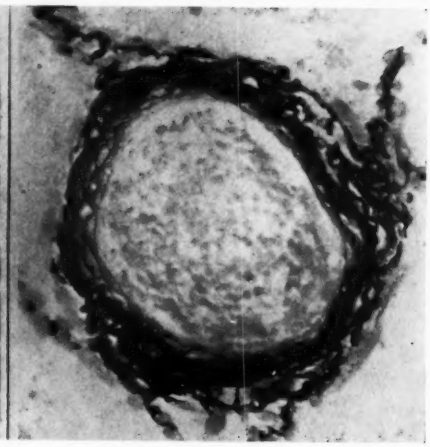

FIG. 6.—Slight, uniform fibro elastic thickening of the intima of a small pulmonary vein. The irregular arrangement of elastic layers in the venous wall can be seen. ×350: Hart-van Gieson.

DISCUSSION

Sclerotic changes occurring in the small pulmonary vessels with increasing age have been studied by Brenner (1935), Welch and Kinney (1948), and Neely (1949) among others. The change found in arterioles and venules was fibrous intimal thickening similar to that here described in both series. Musculo-elastic and fibrous intimal thickening of small arteries have been described in the absence of mitral stenosis and a good account of their development was given by Giroux (1910). Some authors (Eliaschewitz, 1931) have thought that the development of a layer of longitudinal smooth muscle fibres and elastic tissue represents a medial hypertrophy, but we consider this is present only when there is an increase in thickness of the circularly directed muscle. Sclerotic venous changes have received less attention but Brenner described intimal fibrosis with age and fibro-elastosis in congestive failure.

A variety of factors have been thought to play a part in the development of vascular sclerosis, but there is little evidence to support any as of primary or contributory importance, except age and pulmonary hypertension.

Those authors who have concerned themselves more specifically with the vascular changes occurring in mitral stenosis show little agreement as to their nature or significance. Yater and Constam (1928) described thickening of the media of the pulmonary " arterioles " in a case of mitral stenosis with emphysema, and thought this was a primary vascular change that was not related to the other lesions present.

Parker and Weiss (1936) examined 23 cases of mitral stenosis and found proliferative thickening of arteriolar walls with occasional necrotizing arteriolitis and medial hypertrophy of the small arteries: the prolonged action of high intravascular pressure, stagnation of blood flow, and œdema was thought to be of importance in producing these lesions. · Larrabee *et al.* (1949) described medial atrophy of arterioles with fibrous intimal thickening and medial hypertrophy of small arteries with intimal thickening (fibrous or muscular). It is obvious that the same terminology is not used in all these papers.

Our results show that two different processes occur in the small pulmonary vessels in mitral stenosis—(1) an increase in circularly directed muscle in the walls of vessels on the arterial side and (2) acceleration of the development of decrescent changes, best seen on the venous side. The first is seen chiefly as muscularization of arterioles—vessels that normally possess no media—but medial hypertrophy of small arteries also occurs. The origin of the new arteriolar muscle is uncertain. It might arise by hypertrophy of occasional muscle cells related to the elastic lamina or from more primitive mesenchymal cells. The irregular structure of the wall of the muscularized vessel suggests the presence of separate groups of circularly running fibres.

The higher incidence of the muscular type of change in cases dying under 40 years of age suggests a direct relationship with the degree of stenosis, and when the proportion of cases showing arteriolar muscularization is related to the degree of mitral stenosis this is confirmed (Table II). Mitral stenosis leads to early pulmonary hypertension (Lenegre *et al.*, 1948; Draper *et al.*, 1951), which must be considered as a possible ætiological factor. Unfortunately the presence or absence of right ventricular hypertrophy is an inadequate basis for deductions of pulmonary pressure. However, since the small pulmonary arteries and arterioles become more like those of the systemic circulation and also those of the pulmonary circulation in the fœtus (Neely, 1949; Edwards and Chamberlain, 1951) increased intravascular pressure would seem to be of importance. Edwards and Chamberlain also found increased muscle development in congenital cardiac defects with a common ventricular outflow, confined to the small arteries. Finally, Neely (1949) has described similar vascular changes in emphysema and in kyphoscoliosis with right ventricular hypertrophy.

Fibrous intimal thickening of arterioles occurs with increasing age. Over the age of 40 years there is little difference in incidence in each series (47% of control and 53% of mitral stenosis cases), but below this age fibrous changes are more common in association with valvular disease (17% of control and 54% of mitral stenosis cases). Since the same proportion of cases of mitral stenosis in both age groups showed fibrous arteriolar sclerosis there is probably little replacement of muscular change by fibrous change with advancing age.

Fibrous arteriolar thickening may be associated with reduced blood flow. Harrison (1948) described involutionary fibrous intimal thickening of vessels under 200 μ external diameter following blocking of the parent vessel by thrombus material in rabbits. In our cases it was most marked in areas of collapsed or fibrosed lung or with great reduction of arterial lumina by intimal thickening, or healed thrombotic occlusion. No direct relationship was found between the frequency of this change and the degree of stenosis.

The onset of intimal changes in small arteries and veins is also accelerated by the presence of the valvular lesion, especially in the latter, although when gross intimal thickening only is considered the same proportions are found in each series (7% of cases of mitral stenosis; 6% of controls). It seems possible that the fibro-elastic thickening of the venous intima might be hastened by over-distension or stagnation of blood following obstruction to free flow.

Some cases of well established mitral stenosis showed none of the above changes in the pulmonary vessels. Investigations of the autopsy records did not reveal any factor that might have prevented congestion in the pulmonary circulation or the development of pulmonary hypertension (e.g. valvular lesions on the right side of the heart; vascular pleural adhesions, permitting drainage into systemic veins) and right ventricular hypertrophy was present in some of them.

Narrowing of the small pulmonary arteries whatever its cause may help to maintain pulmonary hypertension by increasing resistance in the pulmonary circulation (Edwards and Chamberlain, 1951). Edwards and Burchell (1951) described medial hypertrophy and fibrous intimal thickening of small arteries in a case of pulmonary venous obstruction; they thought that the arterial changes might protect the pulmonary capillaries against excessively high pressures and suggested a similar mechanism in mitral stenosis.

Larrabee *et al.* believe that muscular hypertrophy of small arteries in cases of mitral stenosis would increase resistance to pulmonary blood flow, but that this change would be reversible after valvulotomy in the absence of intimal fibrosis or medial scarring. That pulmonary vascular resis-

tance is actually increased in mitral stenosis has been confirmed by Draper *et al.* (1951) who calculated this factor from direct measurements of pulmonary blood pressure and blood flow: they also showed that the resistance fell following valvulotomy.

Our results confirm the labile nature of the important changes in the pulmonary arteries and arterioles and also suggest that a more effective nervous or humoral control of the pulmonary circulation could exist in mitral stenosis. This might help to maintain a raised pulmonary pressure, but would cease to operate with regression of the vascular changes after valvulotomy. Intimal thickening is probably of no importance in maintaining pulmonary hypertension since the same degree of change is seen in elderly subjects in whom there has been no evidence of raised pulmonary pressure.

Summary

The small pulmonary arteries, arterioles, venules, and small veins were studied in 105 cases of mitral stenosis and compared with those in 67 controls in whom no known or suspected cause of pulmonary hypertension was present.

Diffuse muscularization of pulmonary arterioles associated in some cases with medial hypertrophy of the small arteries was present in 40 per cent of the mitral stenosis but in none of the control cases. The percentage of cases showing this was related to the severity of the stenosis. The development of decrescent changes in the pulmonary vessels especially on the venous side was found to be accelerated by mitral stenosis. In some cases of well established mitral stenosis, however, the small pulmonary vessels were normal.

The increased muscularity of small arteries and arterioles may help to maintain pulmonary hypertension, especially since the pulmonary arterial tree is probably rendered more susceptible to the action of neurogenic or humoral agencies tending to produce pulmonary hypertension. Increased resistance due to muscularization of arterioles is unlikely to persist following mitral valvulotomy. Intimal thickening of the small pulmonary vessels probably plays no part in maintaining pulmonary hypertension.

I would like to thank Professor Biggart for helpful advice and criticism throughout the preparation of this paper, Dr. J. F. Pantridge for suggesting the investigation, and Dr. R. A. Neely for allowing me full access to his thesis; also Mr. J. Davidson and Mr. D. Mehaffey for preparation of the histological material and photography.

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VENTRICULAR WEIGHT IN CARDIAC HYPERTROPHY

BY

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Ventricular hypertrophy is usually estimated at necropsy by weighing the heart as a whole and by measuring the thickness of the ventricular walls. The weight of the heart as a whole is open to the objection that a large and varying proportion of the weight is accounted for by structures other than the myocardium, and the thickness of the ventricular wall is not a satisfactory criterion because it may be greatly modified by dilatation of the cavity. The traditional methods are particularly unsatisfactory when used to assess slight or moderate hypertrophy of the right ventricle.

In an attempt to overcome these difficulties, Müller (1883), Lewis (1914), and Herrmann and Wilson (1922) stripped off non-myocardial tissue and subsequently divided the myocardium into right and left parts. Their techniques are time-consuming, however, and the methods of dividing the septum are open to question so that they have not come into general use. The present investigation is an attempt to evolve a simpler technique for measuring hypertrophy of each ventricle separately, with the special object of assessing lesser degrees of right ventricular hypertrophy.

METHODS

Technique and Division of Hearts. The method described here is a modification of that employed by Lewis (1914). From the results obtained with this method, the simpler technique to be described later was developed. The heart, aorta, and lungs were removed intact from the thorax: the lungs were then separated from the heart, leaving as much as possible of the pulmonary vessels attached to the heart. After inspection for congenital and other lesions of the great vessels, the aorta and pulmonary artery were divided about 1 cm. above the semilunar valves, which were examined. The atria were then opened posteriorly, and the blood clot washed out from the atrial and ventricular cavities. After examination of the mitral and tricuspid valves and the interior of the atria, the heart was packed with cotton wool to maintain its shape, and immersed in 10 per cent formol saline for 72–96 hours. At the end of this time, the coronary arteries were dissected free and opened up. The heart was stripped of vessels and external fat by sharp dissection, leaving the myocardium exposed, and the cotton wool packing was removed. The atria were separated from the ventricles at the atrio-ventricular ring, leaving the isolated ventricular myocardium.

The tendon of the infundibulum was next divided, allowing the pulmonary conus to fall away from the septum, and exposing the anterior junction of the free wall of the right ventricle and the septum The free wall of the right ventricle was separated from the septum with scissors, beginning at the anterior base of the septum and cutting down to the apex, and up the posterior margin of the septum. The cut was made so that the cut surface was in the same plane as the right ventricular surface of the septum. The junction of the comparatively thin right ventricular wall with the septum was easily defined and usually formed an acute angle. Separation was easy, and there was little opportunity for personal error. Trabeculæ on the right ventricular aspect of the septum were cut off at their base: this involved additional trimming when the trabeculæ were hypertrophied, as they were in hearts with marked right ventricular hypertrophy. In a similar way, the free wall of the left ventricle was separated from the septum, but this was more difficult, for the left ventricle and septum form an almost circular band of muscle of roughly the same thickness and the junction of the two is ill-defined. The final cut surface was in the same plane as the flat central portion of the left ventricular aspect of the septum, but additional trimming was always required, and there was room for appreciable personal error. Finally, the valve cusps and the remaining parts of the aorta and pulmonary artery were removed and the three pieces of myocardium (free wall of right ventricle, free wall of left ventricle, and the septum) were weighed on a balance, accurate to 0·5 g.

The possibility of a change in weight due to fixation was considered. Müller (1883) obviated this possibility by dividing the heart in a fresh state, but this makes the dissection much more difficult. Lewis (1914) took great care to restore the original weight of the heart after fixation by successive immersions in formalin, spirit, and water. Herrmann and Wilson (1922) found that prolonged immersion in formalin could cause a loss of weight of over 10 per cent. In our series, however, fixation was not continued for more than four days and in that time the weight of the cardiac muscle did not vary by more than 2 per cent. Consequently, we have felt justified in ignoring the effects of fixation upon the recorded weights.

Classification of Material

We examined 202 hearts and classified them into 4 groups. The basis of the classification was a clinical one, but the diagnosis of valvular lesions and of myocardial infarction was subject to necropsy confirmation.

Group 1. *Normal* (43 hearts). There was no evidence of heart disease either clinically or at necropsy. Hearts from patients over 65 years of age were not included in this group.

Group 2. *Isolated Right Ventricular Hypertrophy* (46 hearts). There was a clinical cause of hypertrophy of the right ventricle alone. The cases comprised chronic cor pulmonale * (37), isolated mitral stenosis (7), and mitral stenosis with a tricuspid lesion (2).

Group 3. *Primary Left Ventricular Hypertrophy* (46 hearts). A cause of primary left ventricular hypertrophy was present clinically, but there was no known cause of independent right ventricular hypertrophy. The cases comprised hypertension (38), isolated aortic lesions (6), and pure mitral incompetence (2).

Group 4. *Miscellaneous* (67). This group consisted of apparently normal hearts from patients over 65 years of age (33), cases where there were lesions liable to cause independent hypertrophy of both ventricles (10), myocardial infarction (6), and unclassified cases (18). It soon became clear that the cases in this group were unsuitable for detailed study, and as the investigation progressed, only hearts that could be included in the first three groups were dissected.

Results

Group 1. *Normal Hearts.* Fig. 1 shows the distribution curves of the total ventricular weight and the weights of the three sub-divisions of the myocardium in the normal group. Table I shows the maximum, minimum, and mean weights with suggested upper limits of normality for each part.

Group 2. *Isolated Right Ventricular Hypertrophy.* This group was divided into patients who died with congestive heart failure (35) and those who died from some other cause (11). Table II shows the maximum, minimum, and mean weights of the various parts of the heart in this group, and indicates the frequency with which each part was above the normal maximum weight.

TABLE I

The Range of Weight in Normal Hearts

Part of the heart	Weight (grams)			
	Maximum	Minimum	Mean	Suggested upper limit of normal
Free wall of right ventricle (R. V.)	68	23	46	65
Free wall of left Ventricle (L.V.)	123	48	86	125
Septum (S)	61	17	39	60
Total ventricular weight (T.V.W.)	235	88	171	250

* The striking preponderance of cases of chronic cor pulmonale was due to the nature of the hospital material, the fact that the investigation took place during the winter months, and that a concurrent investigation concerning chronic cor pulmonale led to a very high necropsy rate in fatal cases.

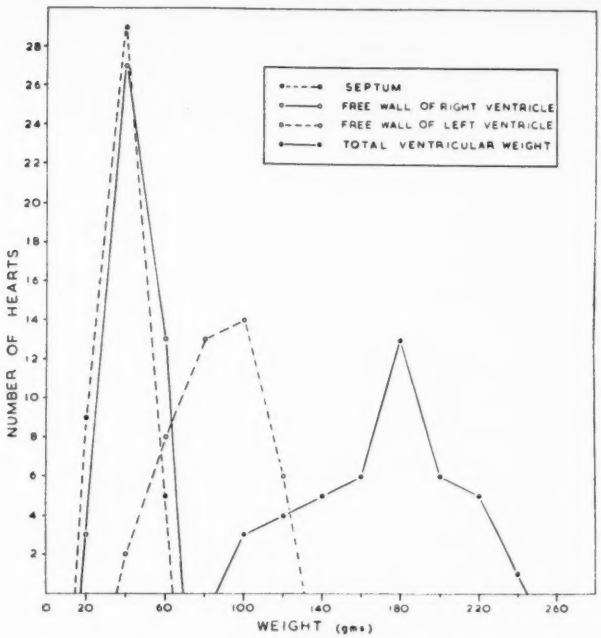

FIG. 1.—Normal hearts: Distribution curves of the total ventricular weight and the weights of the three sub-divisions of the myocardium.

TABLE II

THE RANGE OF WEIGHT IN RIGHT AND LEFT VENTRICULAR HYPERTROPHY

Part of heart	With congestive heart failure				Without congestive heart failure			
	Weight (grams)			Percentage exceeding normal weight	Weight (grams)			Percentage exceeding normal weight
	Max.	Min.	Mean		Max.	Min.	Mean	
Isolated right ventricular hypertrophy								
R.V.	178	59	105	97	105	55	79	72
L.V.	139	59	100	9	117	70	97	0
Septum	70	30	53	31	60	37	49	0
Total	384	173	258	54	274	186	226	27
Primary left ventricular hypertrophy								
R.V.	151	59	96	94	90	35	59	29
L.V.	346	144	217	100	280	121	172	93
Septum	146	54	90	94	125	42	74	74
Total	606	287	403	100	465	220	306	87

Group 3. *Primary Left Ventricular Hypertrophy.* This group was similarly divided into patients who died with (15) and without (31) congestive heart failure. Table II shows the maximum, minimum, and mean weights of the various parts of the heart, indicating the frequency with which each part was overweight.

Discussion

Normal Hearts. The average normal weights in the present series correspond fairly closely with those of other workers (Table III). Both Lewis (1914), and Herrmann and Wilson (1922) found that the normal range for the ratio of left to right ventricular weight was from 1·5 : 1 to 2·2 : 1, a range which includes all but three of our cases. Neither, however, gave a range of normal for the actual weights of the separate parts of the myocardium. As the ratio may in itself be misleading (as, for example, when there is hypertrophy of both ventricles giving a normal ratio), it is essential to consider the actual weights in coming to a decision about the presence or degree of hypertrophy.

Isolated Right Ventricular Hypertrophy. Hypertrophy was found to be practically confined to the free wall of the right ventricle in this group (Fig. 2, Table II). Even in cases with failure, the total ventricular weight was only above the normal range in about half the cases, and the left ventricle and septum were overweight in only 9 and 31 per cent of cases respectively, and then only to a slight extent.

Primary Left Ventricular Hypertrophy. Increase in the weight of the left ventricle was associated with an increase in the weight of the septum and in the total ventricular weight (Fig. 2B, Table II). In cases with failure, the right ventricle was overweight in almost every case, and even in cases without

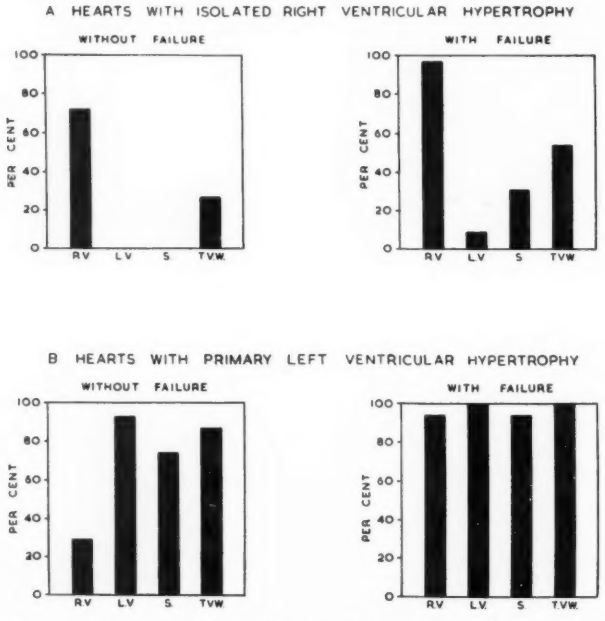

FIG. 2.—The heights of the black columns indicate the percentage of cases in which the weight of the corresponding part of the myocardium exceeded the upper limit of normal. (A) In hearts with isolated right ventricular hypertrophy. (B) In hearts with pulmonary left ventricular hypertrophy. R.V.—right ventricle. L.V.—left ventricle. S—septum. T.V.W.—total ventricular weight.

TABLE III

AVERAGE WEIGHTS IN PRESENT SERIES COMPARED WITH THOSE OF PREVIOUS WORKERS

Author	No. of cases	Average age (years)	Average weight (grams)				Average ratio L.V.: R.V.
			R.V.	L.V.	Septum	Total	
Lewis (1914)	16	33	49	87	23	159	1·74 : 1
Herrmann and Wilson (1922)*	23	41	45	82	25	152	1·81 : 1
Present Series	43	49	46	86	39	171	1·9 : 1

* Allowance has been made for an average loss of 18 g. in total ventricular weight due to prolonged storage in formalin.

failure, the right ventricle was above the upper limit of normal in about one-third of the cases although there was no independent cause of right ventricular hypertrophy. This bears out the finding of Thompson and White (1936) that the commonest cause of right ventricular hypertrophy is left ventricular failure, and our figures illustrate the development of right ventricular hypertrophy in such cases before right heart failure occurs.

Total Ventricular Weight as a guide to Hypertrophy. From the results of this investigation, a total ventricular weight of over 250 g. may be taken as evidence of cardiac hypertrophy. If left ventricular hypertrophy is suspected, this criterion alone is sufficiently accurate, for practically all cases of suspected left ventricular hypertrophy had a weight greater than 250 g., and the amount by which this weight was exceeded paralleled the degree of left ventricular hypertrophy present. If, however, right ventricular hypertrophy alone is suspected, the total ventricular weight is of little value. Even when isolated right ventricular hypertrophy led to congestive heart failure, the total ventricular weight was within normal limits (less than 250 g.) in half the cases. The total heart weight as usually estimated at necropsy is, of course, even more misleading, as it may include up to 100 g. of non-myocardial tissue. We regard separate weighing as the only accurate way of estimating isolated right ventricular hypertrophy.

The Septum in Cardiac Hypertrophy. The septal weight exceeded the upper limit of normality (60 g.) in only 31 per cent of cases of isolated right ventricular hypertrophy with failure, and in cases without failure, the septal weight was invariably within normal limits (Fig. 2, Table II). The increase in weight when present was only slight, and in no case did the septum weigh more than 70 g. (Fig. 3). In hearts with left ventricular hypertrophy, on the other hand, the septum was overweight in 80 per cent of all cases (Fig. 2, Table II) and the increase in weight was often considerable (Fig. 3). Thus in our cases of acquired heart disease, striking septal hypertrophy occurred only in association with left ventricular hypertrophy. We do not suggest that this is universally true, for it is a matter of common observation that when very great right ventricular hypertrophy occurs in congenital heart disease, the septum may also be greatly hypertrophied. From the data in our cases there is no reason to suppose that the septum does not increase in proportion to the increase in the weight of the free wall of *either* ventricle. The apparent discrepancy illustrated in Fig. 3 can be explained by the fact that in our cases the increase of weight of the right free wall is usually much smaller than the increase of weight of the left free wall.

In any method of dividing the heart into right and left sides, the allocation of the septal weight has proved difficult. Müller divided the septal weight between right and left sides in proportion to the weight of the free walls. Lewis included a slice of septum with both ventricles, giving two almost completely closed cavities and a small strip of septum. (This accounts for his average septal weight being much less than ours). In comparing the weights of the two ventricles, he ignored the strip of septum. Herrmann and Wilson, in their method B, cut serial horizontal sections of the ventricles, and divided each slice into a right and left half, cutting along a white line in the septum,

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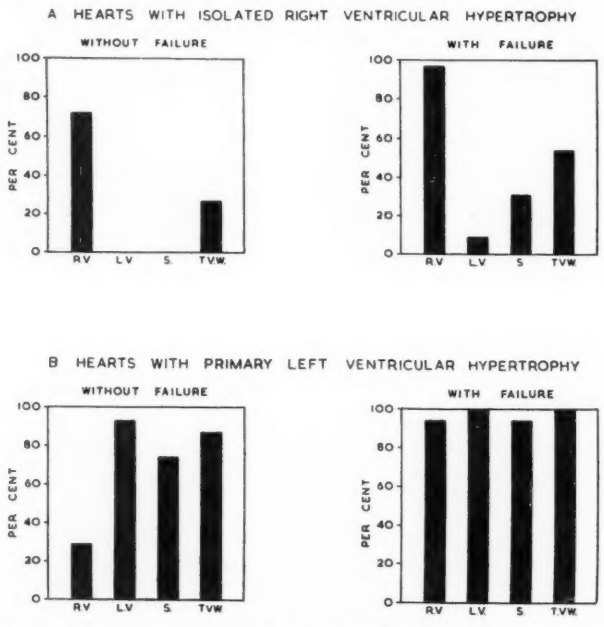

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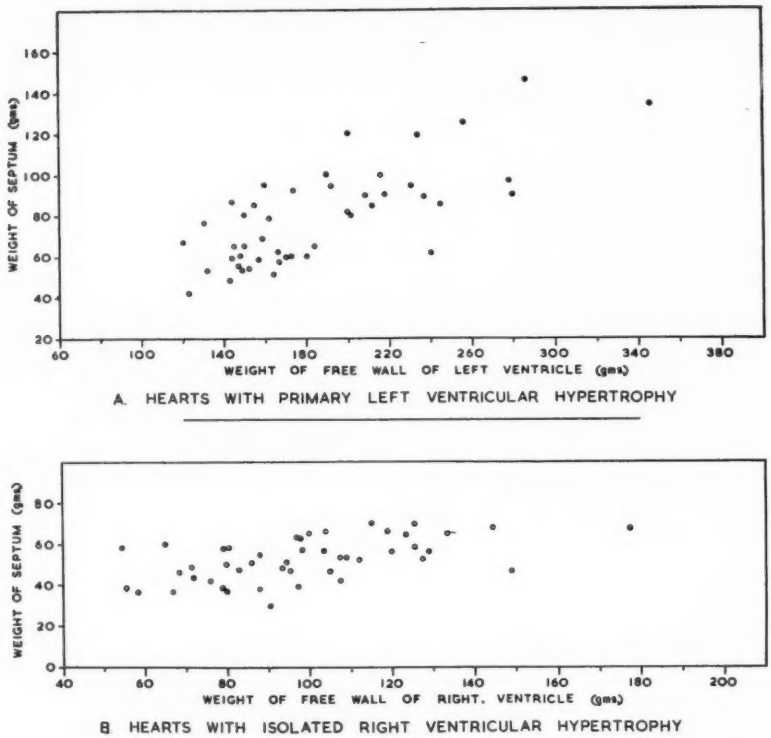

FIG. 3.—Septal weights in (A) Primary left ventricular hypertrophy, and (B) Isolated right ventricular hypertrophy.

which, in their opinion, divided the septum into two halves belonging functionally to the right and left ventricle. This white line, however, if followed backwards and forwards can be traced right round the left ventricle some distance inside the epicardial surface. Herrmann and Wilson's assumption may not be true.

In view of our finding, that in acquired heart disease the septum was never greatly increased in weight except in the presence of left ventricular hypertrophy, it seemed reasonable to consider the free wall of the left ventricle and the septum together as one part of the heart. This has the great advantage of technical simplicity in division, as separation of the free wall of the right ventricle from the rest of the heart is easy and accurate, whereas separation of the free wall of the left ventricle from the septum is difficult and open to error.

The upper limit of normal weight of the free wall of the left ventricle and septum together we regard as 190 g., and the normal range for the ratio of left ventricular plus septal weight to the weight of the free wall of the right ventricle (L+S/R) was found to be from 2·3 : 1 to 3·3 : 1.

Consideration of the heart weights in the present series in this simplified way shows satisfactory agreement with the results of the more detailed dissection. It is suggested, therefore, that after fixation, the free wall of the right ventricle should be separated from the rest of the heart as already described, and that the two pieces—first the free wall of right ventricle and secondly the free wall of left ventricle and septum together—should then be weighted. Using this method our criteria for normality and for right and left ventricular hypertrophy are as follows.

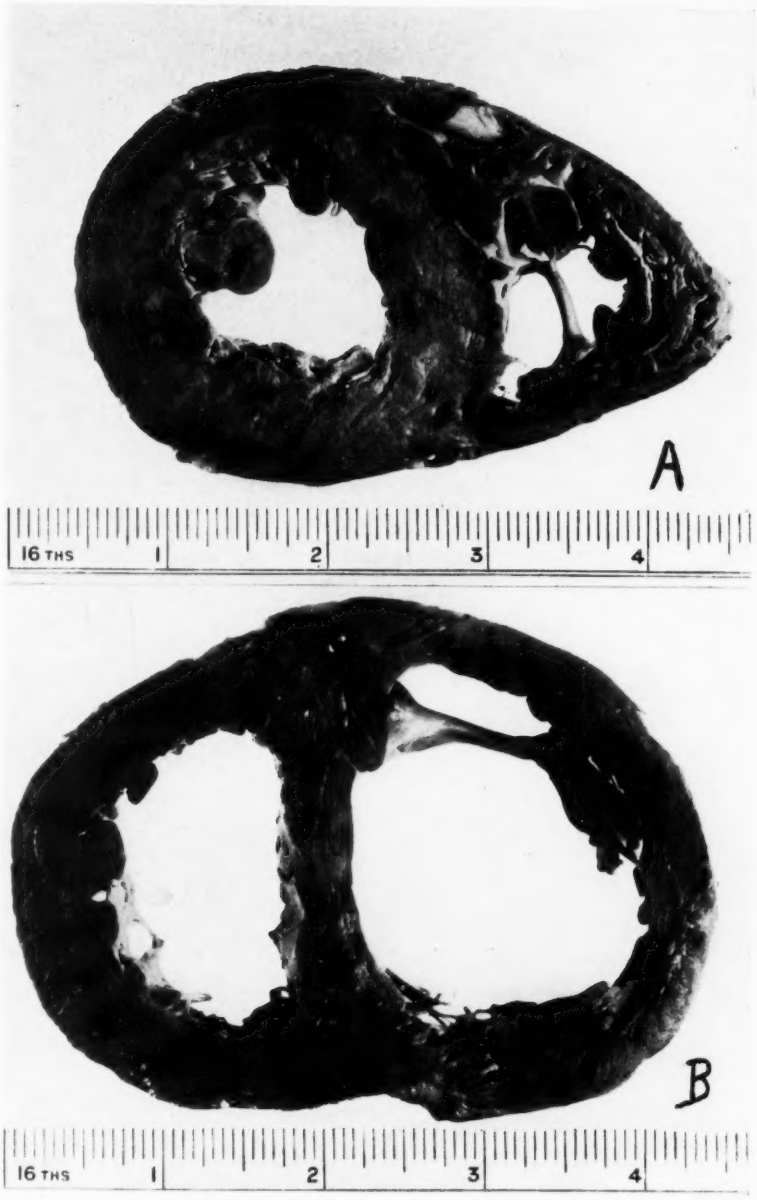

FIG. 4.—Transverse sections through two hearts. (A) with primary left ventricular hypertrophy, and (B) with isolated right ventricular hypertrophy.

Criteria for Normality. A heart may be classed as normal only if

(*a*) the total ventricular weight is less than 250 g.,
(*b*) the free wall of the right ventricle weighs less than 65 g.,
(*c*) the left ventricle and septum together weigh less than 190 g., and
(*d*) the ratio L+S/R lies between 2·3 : 1 and 3·3 : 1.

Criteria for Right Ventricular Hypertrophy. Right ventricular hypertrophy is considered to be present when the free wall of the right ventricle weighs 80 g. or more. In isolated right ventricular hypertrophy the ratio L+S/R is always less than 2 : 1. If left ventricular hypertrophy is also present, the ratio may be within normal limits or even raised.

Criteria for Left Ventricular Hypertrophy. Left ventricular hypertrophy is considered to be present when the weight of the left ventricle plus septum is 225 g. or more. The ratio L+S/R may be modified by secondary or independent right ventricular hypertrophy and the ratio alone is therefore not an indication either of the presence or degree of left ventricular hypertrophy.

Summary

In an attempt to find a satisfactory way of estimating ventricular hypertrophy, 202 hearts were examined. The total ventricular weight and the weights of the free walls of right and left ventricles and of the septum are discussed in relation to normal hearts and hearts with isolated right ventricular hypertrophy and primary left ventricular hypertrophy.

In hearts with left ventricular hypertrophy, the total ventricular weight is always above normal, and is a measure of the degree of left ventricular hypertrophy present. In hearts with isolated right ventricular hypertrophy, the total ventricular weight is within normal limits in 50 per cent of cases, even when congestive failure has been present.

Septal hypertrophy is much commoner and more pronounced in left ventricular hypertrophy than in right.

A simple separation of the heart into two parts, (*a*) the free wall of right ventricle and (*b*) the free wall of left ventricle and septum together, appears to give as accurate an assessment of the site and degree of ventricular hypertrophy as is possible by more elaborate methods.

Criteria for the recognition of normality and of right and left ventricular hypertrophy are suggested.

We wish to acknowledge our indebtedness to Dr. J. V. Davson, Pathologist to the North Manchester Group of Hospitals, and to his Staff at Crumpsall Hospital, for most helpful co-operation which made this investigation possible.

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HEART DISEASE IN SCLERODERMA

BY

D. W. BARRITT AND W. O'BRIEN

From Charing Cross Hospital

Received October 15, 1951

The lesions of scleroderma are now recognized to be widespread throughout the body. The œsophagus, the gastro-intestinal tract, and lungs are commonly involved besides the skin and muscles. The nerves and central nervous system, the endocrine glands, bones, joints, and the mouth (the tongue and palate) may also be affected. Pathological changes in the heart muscle have long been recognized at necropsy in these cases, but clinical signs of cardiac involvement appear to be rare. Heine in 1926 was the first to describe such a case; Weiss in 1943 collected nine cases, whilst Mathison and Palmer (1947) in America and East and Oram (1947) in this country have each described a case.

Case Reports

Case 1. A single woman, aged 50 years, working as a dressmaker developed herpes zoster in 1946 and following this never regained her previous good health and began to notice for the first time breathlessness on exertion. In 1948 the typical lesions of scleroderma appeared spreading to involve the hands, arms, face, buttocks, and legs and this was accompanied by conspicuous general muscular weakness. In the beginning of 1951 this breathlessness increased so that she would have to stop and look into shop windows to recover while walking. In April, 1951, swelling of both ankles appeared. She was admitted into Charing Cross Hospital in May.

On admission it was found that there were widespread sclerodermatous skin lesions with heavy pigmentation involving the hands, arms, face, buttocks, and legs with scars of recent small ulcerations on the tips of the fingers (Fig. 1). The jugular venous pressure was considerably raised, there were rales at both lung bases, the free margin of the liver was felt at the level of the umbilicus, and the legs and sacrum were œdematous. The pulse rate was 100 a minute, the rhythm regular and no pulsus paradoxus was detected. The apex beat was displaced far out and was moderately vigorous; the first heart sound was widely split at the apex and the second heart sound widely split at the base; there were no murmurs. The blood pressure was 155/80.

Radioscopy showed the heart to be greatly enlarged and triangular in shape, with little movement (Fig. 3). The appearances were suggestive of a pericardial effusion whilst a kymogram confirmed the lack of movement of the ventricles. An X-ray of the hands showed calcinosis of the fingers (Fig. 4). The electrocardiogram revealed depression of the S–T segment over the left ventricular leads with flat T waves. The S–T segments from V2 to V4 were elevated with the concavity of the curve upwards (Fig. 2).

The temperature remained normal. The E.S.R. was 80 mm. in the first hour. No fluid was obtained from the pericardium though paracentesis was twice attempted.

Laboratory investigations. Blood examination: hæmoglobin 11·4 g. W.B.C., 3600; polymorphs, 79 per cent. No eosinophils were found in 1 c.mm. of blood. Plasma proteins, 8·4 per 100 ml. (albumin, 3·9; globulin, 4·5). Sodium, 324; chlorides, 609; calcium, 8·7 (mg. per 100 ml.). Pyruvate levels within normal range. Urinary creatinine, 3·9 g; creatine, 4·5 g. per 100 ml.

FIG. 1.—Case 1. Generalized scleroderma.

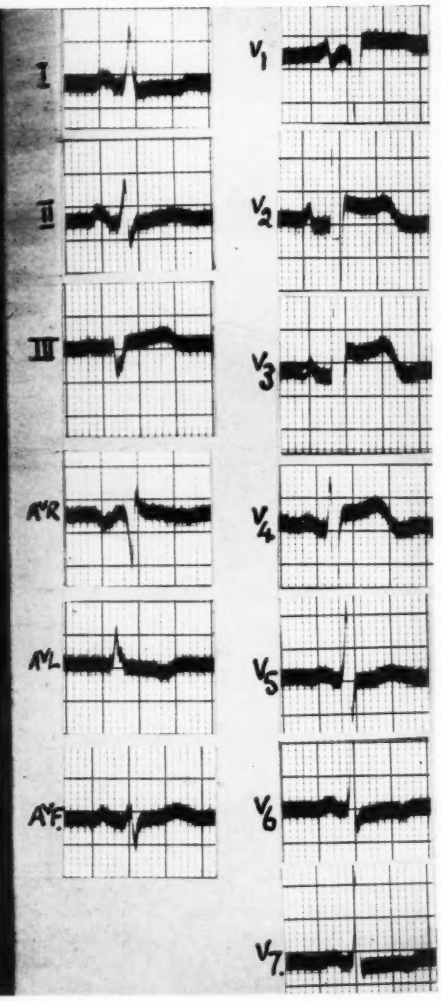

FIG. 2.—Case 1. Cardiogram in scleroderma heart disease.

Skin and muscle biopsy report. "The sections of the skin showed increased fibrosis of the dermis and collections of plasma cells and eosinophils. The muscle showed slow necrosis with fibrous replacement. The condition appeared to be dermatomyositis."

Progress. The patient was treated with digitalis and neptal and with salt and water restriction, and in the first three weeks her œdema subsided and the jugular venous pressure fell, though it remained raised. In the hope of influencing the sclerodermatous process a course of A.C.T.H. was begun and she was given 25 mg. four times daily for twelve days. The dose was later reduced to 15 mg. four times daily for twenty-five days. The eosinophil count showed a satisfactory response. Within a few days of starting A.C.T.H. therapy she felt better, her muscular strength

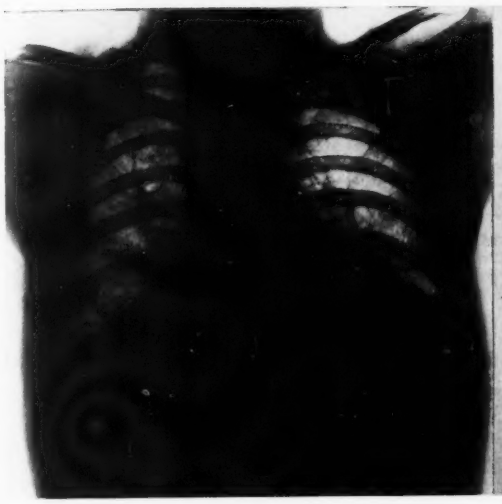

FIG. 3.—Case 1. Teleradiogram in scleroderma heart disease.

FIG. 4.—Case 1. X-ray of hands showing atrophy of terminal phalanges and calcinosis.

was a little greater and the limitation of movement of the elbows was reduced though not abolished. As hormone therapy ceased, the jugular venous pressure was still raised and rales were heard at the lung bases. A week later, however, the venous pressure had fallen to normal, the lung bases were clear, and congestive failure was considered no longer to be present. This result was not unexpected in view of the salt and water retention effect of A.C.T.H. A great improvement was evident in the general condition of the patient. She began to walk again; the skin of the face lost much of its pigmentation and she was able to begin to knit.

The electrocardiogram was unchanged. There was no significant change in the size and shape of the heart.

Case 2. A housewife of 44 years had symptoms for seven years. She first noticed weakness of the arms with discoloration and tightening of the skin. The ankles began to swell and there were wide-spread pains in the limbs and trunk. For six years flexion deformities of the knees had prevented her from walking. In the last three years her condition had improved rather than deteriorated and she was able to move about the room on a wheel stool. Her mother had been a diabetic.

Clinical examination showed classical sclerodermatous lesions of the arms, neck, trunk, and legs. There were flexion deformities of both elbows and knees with considerable muscular weakness. The pulse was regular, and of normal volume. B.P., 130/70. The cardiac impulse was not displaced and was of normal left ventricular type. The first and second heart sounds were normal at the apex and base. The jugular venous pressure was not raised. The lung bases were clear. The urine contained glucose.

Radioscopy showed a normal cardiac silhouette, and the barium swallow was normal. The cardiogram showed inversion of the T waves in leads V1 to V4 (Fig. 5).

The following pathological data were obtained: Glucose tolerance curve was of the diabetic type. Urinary creatine was 70 mg per 100 ml. Creatinine was 37 mg. per 100 ml.

Progress. The patient's condition was slowly improving and it was not felt justified to subject her to A.C.T.H. therapy. The diabetes was known to have been of recent onset and responded

satisfactorily to a low carbohydrate diet. The presence of a family history of diabetes made it unlikely that sclerodermatous fibrosis of the pancreas was responsible for her glycosuria.

Discussion

The coincidence of cardiac failure and scleroderma does not prove that they are related but in these cases the evidence for such an assumption is strong. The absence of a history of rheumatism, chorea, or anginal pain, the absence of signs of a valvular lesion in the heart, of hypertension, of thyroid disease, of anæmia, of pulmonary disease, or of vitamin B deficiency ruled out anything but a rare cause of the congestive failure. In reports of necropsies in this condition gradual replacement of the heart muscle fibres with fibrous tissue without evidence of an inflammatory reaction appears to be the basic lesion. The subepicardial muscle is the region most affected and the fibrosis may extend to the subepicardial fat and subepicardial connective tissue. A variable pericardial effusion may be found and a chronic fibrous pericarditis was present in Bevan's case (1945). In the first case, progressive cardiac failure in normal rhythm associated with a characteristic triangular shape of the heart, and lack of ventricular movement, with non-specific electrocardiographic changes suggested pericardial involvement. This may be the usual picture. These were two of four cases of generalized scleroderma present in the hospital at the same time suggesting that cardiac involvement is by no means rare.

A.C.T.H. produced a general improvement in Case 1, and congestive heart failure was relieved when a long period of rest, dieting, and medication had been only partially successful. It is clearly justifiable to administer this compound in scleroderma heart disease provided proper precautions are taken to prevent sodium and water retention.

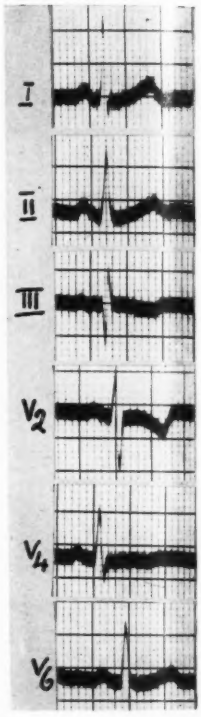

FIG. 5.—Case 2. Cardiogram in scleroderma heart disease.

Summary

Two cases of scleroderma heart disease are described. Reference is made to the apparent rarity of severe circulatory changes in this condition. Congestive heart failure was present in one of the cases. Treatment with A.C.T.H. did not produce any remarkable change in the heart condition.

We wish to thank Dr. R. A. Hickling and Dr. K. Shirley Smith for permission to study their cases.

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ABSTRACTS OF CARDIOLOGY

Aminophylline as Supplement to Mercurial Diuretics in Intractable Congestive Heart Failure. A. VOGL and P. ESSERMAN. *J. Amer. med. Ass.*, **147**, 625–630, Oct. 13, 1951.

The authors claim that aminophylline is of value as a supplement to mercurial diuretics in the treatment of dropsy due to chronic congestive heart failure.

The technique recommended is the administration by slow intravenous injection of 0·5 g. aminophylline mixed with a mercurial diuretic on the morning of the first day, and thereafter 5 injections of aminophylline alone at 12-hourly intervals. It is pointed out that 0·5 g. is the smallest useful daily dose; a larger dosage may be required in many cases, but not more than 0·5 should be given at any one time. The injections should be made slowly with the patient recumbent, signs of danger being increased depth and rate of respiration.

G. F. Walker

The Myth of Strict Bed Rest in the Treatment of Heart Disease. S. A. LEVINE. *Amer. Heart J.*, **42**, 406–413, Sept., 1951.

Physiological and clinical observations are discussed to show that strict rest in bed is deleterious to patients with congestive heart failure, and that rest in an armchair with the feet down is far preferable. The patient should observe the same rest in a chair with arm and foot rests as is usual in treatment in bed. The position assumed in a chair encourages accumulation of fluid in the legs and thereby diminishes pulmonary congestion. It is also suggested that 8- or 9-in. (20- to 22·5-cm.) blocks be placed under the headposts of the bed during the patient's rest in bed at night. The advantages of treatment in a chair over that in a cardiac bed are pointed out. All other measures of cardiac treatment are carried out in the usual way. Chair treatment has also been successfully employed by the author in cases of coronary thrombosis. The only exception, and the main contraindication, to this method of treatment is the presence of significant shock.

A. Schott

Young Candidates for Coronary Heart Disease. M. M. GERTLER, S. M. GARN, and P. D. WHITE. *J. Amer. med. Ass.*, **147**, 621–625, Oct. 13, 1951.

According to the authors, not only is it possible to "preselect" a young man likely to have coronary heart disease, but at least something can be done to shield him from his peril. In support of this remarkable claim they present a study of 100 young sufferers from proven coronary disease on whom they carried out a variety of clinical and biological tests, the results of which were compared with those in a similar but somewhat larger group of men entirely free from coronary disease. Their findings led them to deduce that young men of resolute and intensive personality, of stocky physique, with a serum cholesterol level above 309 mg. per 100 ml., a serum uric acid concentration of more than 5·4 mg. per 100 ml., and a total cholesterol–lipid phosphorus ratio above 22·5 are likely to suffer from coronary disease. As practical preventive measures in such subjects the authors recommend either lowering the serum cholesterol level or raising the serum phospholipid level. The authors regard the latter as likely to be clinically the most useful and effective.

[This paper contains much careful and original work and is worth reading in full.] *G. F. Walker*

Treatment of Angina Pectoris with Propylthiouracil. L. WAITZKIN. *Ann. intern. Med.*, **34**, 1107–1125, May, 1951.

In this article from Boston the author describes the criteria for treatment by propylthiouracil in his own series of 7 cases. Propylthiouracil was given only to patients with angina in whom the symptom had been present for more than a year, in whom a constant or decreasing quantity of exercise produced the pain, and in those who did not improve after 4 weeks in hospital. Patients who had recently had cardiac infarction or congestive heart failure were excluded, as also were those in whom the angina was not due to arteriosclerosis.

The usual dose of the drug was in the region of 1 to 3 g. a day, but no standard dose was found to suit all patients. Frank myxœdema must be produced to get the full effect with puffiness round the eyes, and this takes 2 to 3 months. The mechanism of improvement is not known, but it does not bear a direct relationship to a lowering of the basal metabolic rate and may have some connexion with the decline in circulating thyroxine. On the whole the treatment was successful, giving several months of pain-free existence to patients who would otherwise have been severely disabled.

G. S. Crockett

Myocardial Infarction with and without Acute Coronary Occlusion. A Pathologic Study. R. D. MILLER, H. B. BURCHELL, and J. E. EDWARDS. *Arch. intern. med.*, **88**, 597–604, Nov., 1951.

In a study at the Mayo Clinic of 143 cases of recent myocardial infarction 49 were found to have no acute occlusion of a coronary artery. The percentage of such cases in similar series reported varies; Foord (*J. Amer. med. Ass.*, 1948, **138**, 1009), after a particularly careful examination of the arteries, found only 41 of 264 cases of myocardial infarction without an occluding thrombus. There may be some doubt about the significance of thrombi that are so hard to discover. The present

authors point out that of the cases of coronary insufficiency without occlusion almost as many were in women as in men, and refer to a similar finding by Gross and Sternberg (*Arch. intern. Med.*, 1939, **64**, 249). This sex incidence is very different from that where the infarction of the myocardium is accompanied by an easily found recent occlusion of a major coronary artery.

In patients with coronary insufficiency there was much more evidence of cardiac hypertrophy than among those with occlusion, and the authors state that hypertension, previous attacks of cardiac failure, and the presence of old infarctions of the myocardium seemed more frequent in the group with coronary insufficiency. It is interesting that in the latter group there was no higher incidence of pulmonary embolism, post-operative shock, or of calcific stenosis of the aortic valve. The degree of sclerosis of the coronary arteries was equal in the two groups, but this has not been correlated with the cardiac weights, as has been done by previous workers, who showed that myocardial infarction from coronary insufficiency was more likely to occur in patients with good coronary arteries if the heart was hypertrophied.

The site of the infarction in the cases of coronary insufficiency was usually anterior and antero-lateral [the greater frequency of severe sclerosis in the anterior descending branch is doubtless of significance here], and the infarction itself was usually subendocardial. The percentage of transmural infarcts was five times greater in the cases of acute coronary occlusion.

A. C. Lendrum

Results of Surgical Treatment of Coronary Disease. M. Fauteux. *Arch. Mal. Cœur*, **44**, 673–686, Aug., 1951.

The author summarizes his experience and results in the surgical treatment of coronary insufficiency in Montreal during the past 10 years by ligation of the great cardiac vein, or denervation of the coronary arteries, or (in most cases) a combination of the two, the former procedure being said to stimulate the development of an adequate collateral circulation in the heart wall, and the latter preventing spasm of the coronary arteries. He claims that this form of surgery is no longer in the purely experimental stage and that the danger of operating on the heart of a patient with coronary insufficiency is no greater than that of the disease itself. The operation is indicated in patients whose condition has failed to improve after a reasonable period of medical treatment. It is contraindicated in patients over 60 years of age and in those with diabetes, recent coronary thrombosis, cardiac failure, or bundle-branch block. On the other hand, evidence of an old coronary thrombosis and the presence of hypertension and cardiac hypertrophy need not be regarded as contraindications.

Of 78 patients between the ages of 36 and 65 who were operated upon, 16 died from a variety of causes either during or within 20 days of the operation and a further 6 died 3 weeks to several years after operation from causes apparently unrelated to it. The 56 surviving patients have been followed up for periods ranging from 5 months to 10 years. Of the 37 survivors whose ages at operation were between 36 and 52 years, the great majority are stated to be very well and free of anginal symptoms, all having benefited from the operation. In older patients operative and post-operative mortality was higher, and less improvement in the condition of the survivors was noted. *E. Schiller*

Dissecting Aneurysms of the Coronary Arteries. H. J. Schmid. *Schweiz. med. Wschr.*, **81**, 1170–1172, Dec. 1, 1951.

An illustrated description is given of a very large dissecting aneurysm of the intermediate branch of the left coronary artery. The patient died aged 47 with the signs of severe asthma and emphysema. The aneurysm, not then correctly diagnosed, could be seen clearly on an X-ray film taken 9 years earlier. Even at that time it showed calcification of its wall, proving that it must have been in existence for years before. A malformation at the origin of the intermediate branch was found at post-mortem examination. Of the 38 cases of coronary aneurysm published so far this is the largest aneurysm and the one with the longest history. *L. Michaelis*

Hemoptysis in Mitral Stenosis. A. C. Thompson and W. C. Stewart. *J. Amer. med. Ass.*, **147**, 21–24, Sept. 1, 1951.

Frank hæmoptysis was a symptom in 29 of 168 cases of mitral stenosis. The symptom occurred in patients with no cardiac enlargement and in the total absence of congestive failure, as well as in more severe cases. In the latter it might be due to pulmonary infarction, and in such instances the prognosis was worse. In the less severe cases there was no definite relationship between hæmoptysis and pulmonary œdema. On occasions the hæmoptysis was very profuse.

It is difficult to account for all these cases on a basis of pulmonary hypertension, and suspicion falls on the enlarged communicating venous channels which are said to link the bronchial and the pulmonary circulations. On post-mortem material these channels have been demonstrated running along the lumina of secondary and tertiary bronchi; in this position they are beyond the reach of bronchoscopy. Bronchoscopy in several patients of this series showed no bronchial varices.

It is important to note that, except in the later stages of mitral stenosis, hæmoptysis may be associated with mild circulatory impairment and a reasonably good prognosis. Hæmoptysis cannot be taken as a sign of pulmonary hypertension, and is probably of little value in deciding whether or not surgical intervention is necessary in mitral stenosis. *J. McMichael*

A Haemodynamic Study of Mitral Stenosis. P. Soulié, J. Carlotti, J. R. Sicot, and F. Joly. *Sem. Hôp. Paris*, **27**, 2627–2642, Sept. 10–14, 1951.

Cardiac catheterization was carried out on 36 patients with mitral stenosis, 25 of them having sinus rhythm. In the majority of cases the pulmonary arterial pressure was increased, and in 23 the cardiac output was reduced. No correlation existed between the degrees of mitral stenosis and of reduction in cardiac output. The pulmonary arterial pressure was raised in all cases in which the calculated mitral surface fell below 2 sq. cm. as determined by the formula of Gorlin (*Amer. Heart J.*,

1951, 41, 1). The pulmonary arteriolar resistance and total pulmonary resistance were increased in most cases. On effort, the mean pulmonary arterial and capillary pressures rose, while arteriolar and total resistance fell.

The authors distinguish two types of case. In the first, usually in patients over 30, the pressure gradients between pulmonary artery and pulmonary capillaries is steep, pulmonary arteriolar resistance being high and the pulmonary vascular bed not being used to its maximum capacity. In the second type the pulmonary capillary pressure approaches that in the pulmonary artery, arteriolar resistance being raised little, if at all, and utilization of the pulmonary vascular bed being determined directly by the degree of mitral stenosis present. These younger patients are therefore more liable to develop pulmonary œdema, although in its absence the lung fields are clear and the right ventricle little enlarged.

Leon Cudkowicz

Evaluation of Adequate Antepartum Care for the Cardiac Patient. J. E. FITZGERALD, A. WEBSTER, B. P. ZUMMO, and P. C. WILLIAMS. *J. Amer. med. Ass.*, **146**, 910–914, July 7, 1951.

The authors studied the cases of 704 women with organic heart disease; 24 died, but only 3 of these had had antenatal care in the special cardiac clinic attached to the hospital, and these 3 all died following abdominal hysterotomy. In the whole series death was chiefly due to the complications of rheumatic heart disease, this being the cardiac lesion in 93% of cases. The causes of death are stated to have been endocarditis in 15 cases. It was found that the risk increased with age and the occurrence of decompensation, no matter how mild. Gravidity and parity alone had no influence on the outlook.

The authors outline their methods of antenatal care in these cases. When the patient is in labour the authors stress the routine use of morphine with scopolamine hydrochloride, and the addition of digitalis and oxygen if the pulse rate is over 110 or the respiratory rate over 24. If there is no obstetrical complication they recommend delivering the cardiac patient vaginally, preferably by low forceps extraction under pudendal block analgesia. Pregnant women with cardiac defects are recognized as very poor surgical risks, and in only 8 cases of the present series was the pregnancy interrupted, this proving fatal in 3 cases. After delivery, rest in bed and sedation are continued as long as is considered necessary.

Elaine M. Sunderland

Morbus Coeruleus and its Surgical Treatment. M. CAMPBELL. *Lancet*, **2**, 647–653, Oct. 13, 1951.

Central cyanosis is seen best in the conjunctivæ, on the tongue, and inside the lips, and is due almost always to a right-to-left shunt. This entails a raised pressure in the right side of the heart, and the most common cause of this is pulmonary stenosis.

The following points have been found important in the selection of cases of Fallot's tetralogy for operation: central cyanosis from birth or early infancy; a history of squatting; absence of much cardiac enlargement; a diminished pulmonary second sound; small pulmonary arteries and diminished density of the lung fields on cardioscopy; right ventricular preponderance in the electrocardiogram. In doubtful cases cardiac catheterization will show the grade of pulmonary stenosis through the fall in pressure as the catheter passes into the pulmonary artery; it may also indicate whether the stenosis is valvular or infundibular. Angiocardiograms show clearly a right-to-left shunt either through an auricular septal defect or an overriding aorta. They may indicate that the stenosis is infundibular and not at the pulmonary valve, but they do not help greatly in estimating the degree of stenosis.

Operations consist in a subclavian–pulmonary anastomosis (Blalock) or a pulmonary valvotomy (Brock). The best age for operation is between 5 and 15 years. The results of anastomosis in 110 cases were: good, 73; fair, 17; deaths, 11. Valvotomy must be done when there is a valvular stenosis with a closed ventricular septum, and is an alternative to an anastomosis when the valvular stenosis is part of a Fallot's tetralogy. The results in 54 cases have been: good, 33; fair, 8; deaths, 11; and the mortality has been steadily declining. Resection of the infundibulum has also been undertaken in patients in whom stenosis was severe and the aorta less overriding, as suggested by little cyanosis but much disability. The results in 16 cases have been: good, 8; fair, 2; deaths, 5. Of the whole series the result of operation was classified as " nil " in 12 cases.

[This article contains much more information on the various problems involved than can be put into an abstract, and should be read in full by those interested in the subject.]

C. W. C. Bain

Coarctation of the Aorta. A Study of Seventy Cases in which Surgical Exploration was Performed. O. T. CLAGETT and R. W. JAMPOLIS. *Arch. Surg., Chicago*, **63**, 337–348, Sept., 1951.

In this paper from the Mayo Clinic summaries are given of 70 cases in which the patient had been operated on for coarctation of the aorta during the last 4½ years. The average at which operation was undertaken was 24½ years, the patients ages varying from 7 to 50 years.

The commonest symptoms were tiredness, dyspnœa on exertion, headaches, aching and weakness in the calves, palpitation, cold feet, and precordial pain, in that order.

According to the authors two congenital phenomena are often associated with coarctation—bicuspid aortic valves and cerebral aneurysms. There is occasionally an associated patent ductus arteriosus. Operation is advised if the subject is otherwise fit. The technique of operation is briefly described, and it is pointed out that in many cases where the stricture is long the operation can be brought to a successful conclusion only by the use of aortic grafts. [The results of operation are not evaluated.]

Of the 70 patients, in 8 operation was impossible owing to the length of the stricture, hyperplasia of the aorta distal to the coarctation, aneurysms of the intercostal arteries, or excessive size of these vessels. The mortality rate in the 70 patients was 7%, all the deaths occurring in the first 15 patients operated upon; no deaths occurred after the last 55 operations.

Peter Martin

Cerebral Lesions in Congenital Heart Disease. A Review of Autopsies on One Hundred and Sixty-two Cases. M. BERTHRONG and D. C. SABISTON. *Bull. Johns Hopk. Hosp.*, **89**, 384–401, Nov., 1951.

The authors studied post mortem 162 cases of congenital heart disease—135 of the cyanotic and 27 of the acyanotic type. Both in patients who had been operated upon and in those not treated surgically cerebral lesions occurred much more frequently than in patients without cardiac malformations. The reasons for this finding are discussed, importance being ascribed to the part played by polycythæmia in the causation of infarctions. Brain abscesses are also claimed to occur with increased frequency in these patients. The authors further report a high incidence of congenital aneurysms of the circle of Willis in patients with coarctation of the aorta.

R. B. Lucas

Observations on Cerebral Arteriosclerosis. G. EROS. *J. Neuropath. exp. Neurol.*, **10**, 257–294, July, 1951.

In this investigation a very comprehensive study of the blood vessels of 52 brains, supplemented by a less detailed examination of another 36, was carried out. The diagnosis of cerebral arteriosclerosis was made either clinically or at necropsy. As a result of his findings the author has differentiated two distinct types of arteriosclerotic change in the cerebral vessels. All branches of the cerebral arteries may be affected, from the largest to the small cortical branches.

Clinical records of a number of cases are given, and from these it appears that the " hyperplastic " form of arteriosclerosis is more commonly associated with focal neurological symptoms and hypertension than with mental symptoms, which develop late in the course of the disease.

The clinical manifestations associated with the " hypoplastic " type of cerebral arteriosclerosis are especially those of the mental deterioration, the symptoms often resembling those of schizophrenia. Delusions and hallucinations also occur in many cases, but signs of focal damage are absent.

The author concludes that the primary and most important lesion in cerebral arteriosclerosis is degeneration of the elastic lamina of the vessels, and that this is of the " hyperplastic " or " hypoplastic " type according to an unknown constitutional factor in the vascular system.

Ruby O. Stern

Auricular Fibrillation. M. PRINZMETAL, R. OBLATH, E. CORDAY, H. E. KRUGER, L. A. SMITH, J. FIELDS, R. KENNAMER, and J. A. OSBORNE. *J. Amer. med. Ass.*, **146**, 1275–1281, Aug. 4, 1951.

The authors have examined the auricle by high-speed cinematography and cathode-ray electrocardiography. In man and animals a wave of contraction flows over the auricle from its focus in all types of rhythm except fibrillation. In auricular fibrillation two types of activity occur simultaneously: a fibrillation of microscopic dimensions, and a larger, irregular fibrillation visible to the naked eye. Corresponding electrical activity can be demonstrated on the cathode-ray oscillograph. No evidence of circus movement has been found, and the authors consider that it plays no part in the maintenance of fibrillation. They hold that fibrillation occurs when discharges from an ectopic focus occur at intervals shorter than the time needed for conduction recovery. Quinidine restores regular rhythm by slowing the rate of discharge from the ectopic focus. Digitalis generally increases the rate of discharge, and so perpetuates fibrillation. Both drugs depress auricular conductivity at high auricular rates.

D. Verel

Quinidine Treatment of Auricular Fibrillation. M. J. GOLDMAN. *Amer. J. med. Sci.*, **222**, 382–391, Oct., 1951.

Eighty patients with auricular fibrillation were treated with quinidine. All but 2 of them were males and their ages ranged from 28 to 88 years. Auricular fibrillation had been present from a few days to 30 years. The majority of the patients had congestive failure on admission to hospital, which was treated by usual measures. Quinidine was given in an initial dose of 0·2 g. to test for sensitivity. Following this the usual dose was 0·2 g. 4 times a day, increasing, if the rhythm had not reverted to normal after 3 days, to 0·4 g. and then 0·6, 0·8, 1·0, and 1·2 g. 4 times daily at 3-day intervals. Only rarely was a total daily dose of 6 g. exceeded. When the rhythm returned to normal a maintenance dose of about half that necessary to abolish the auricular fibrillation was prescribed indefinitely.

In all 44 of the " degenerative " cases, in 13 of the 25 rheumatic cases, in all 4 thyrotoxic cases, and in 6 of the unclassified cases the heart rate was restored to normal rhythm. As the majority of the patients were in congestive failure they received digitalis at the same time as quinidine. In 10 cases congestive failure was improved following the return to normal rhythm. Three patients showed evidence of emboli during treatment. The author suggests that quinidine might with advantage be used more frequently in all types of cases of auricular fibrillation.

C. Bruce Perry

Cardiac Beriberi Simulating Arteriosclerotic Heart Disease. P. SCHLESINGER and A. B. BENCHIMOL, *Amer. Heart J.*, **42**, 801–808, Dec., 1951.

The authors, drawing on their experience in Rio Janeiro with 21 cases of beriberi heart disease, state that, since the hyperkinetic circulatory state is not constantly clinically manifest, the four suggestive features that lead to diagnosis are: (1) history of chronic alcoholism; (2) other evidence of vitamin deficiency; (3) absence of other ætiological factors; and (4) improvement with rest and administration of aneurin. At necropsy in 2 cases the important findings were: normal coronary arteries, marked interstitial œdema, central basophilic degeneration in some myocardial fibres, subendocardial fibrosis, and, in one case, peripheral-nerve demyelinization. These features, coupled with the history of chronic alcoholism, were considered sufficient to warrant the diagnosis of beriberi heart disease. Advanced myocardial fibrosis was regarded as the irreversible end-stage of cardiac beriberi and the cause of the unusual electrocardiographic findings in 2 cases.

K. G. Lowe